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=> file biosis caba caplus embase japio lifesci medline scisearch
=> e jacobs jr william r/au
E1            1     JACOBS JR W R JR/AU
E2            1     JACOBS JR WILLIAM/AU
E3          168 --> JACOBS JR WILLIAM R/AU
E4            3     JACOBS JR WILLIAM R JR/AU
E5            1     JACOBS JUCIA F/AU
E6            1     JACOBS JUDE T/AU
E7            5     JACOBS JUDITH/AU
E8            1     JACOBS JUDITH A/AU
E9            1     JACOBS JUDITH H/AU
E10          90     JACOBS JUDITH M/AU
E11           3     JACOBS JUDITH R/AU
E12           6     JACOBS JUDITH R C/AU

=> s e1-e4 and RD1 and auxotroph and pantothenate
L1            1 ("JACOBS JR W R JR"/AU OR "JACOBS JR WILLIAM"/AU OR "JACOBS JR
                WILLIAM R"/AU OR "JACOBS JR WILLIAM R JR"/AU) AND RD1 AND AUXOTR
                OPH AND PANTOTHENATE

=> d

L1   ANSWER 1 OF 1  EMBASE  COPYRIGHT (c) 2009 Elsevier B.V. All rights
     reserved on STN
AN   2007506752  EMBASE   <<LOGINID::20091103>>
TI   Failure of a Mycobacterium tuberculosis .DELTA.  ***RD1***   .DELTA.panCD
     double deletion mutant in a neonatal calf aerosol M. bovis challenge
     model: Comparisons to responses elicited by M. bovis bacille Calmette
     Guerin.
AU   Waters, W. Ray (correspondence); Palmer, Mitchell V.; Nonnecke, Brian J.;
     Thacker, Tyler C.
CS   National Animal Disease Center, Agricultural Research Service, US
     Department of Agriculture, 2300 Dayton Avenue, Ames, IA 50010, United
     States. ray.waters@ars.usda.gov
AU   Scherer, Charles F. Capinos; Estes, D. Mark
CS   University of Texas Medical Branch, Department of Pediatrics, the Sealy
     Center for Vaccine Development, Galveston, TX 77555, United States.
AU     ***Jacobs Jr., William R.***  ; Larsen, Michelle H.
CS   Howard Hughes Medical Institute, Department of Microbiology and
     Immunology, Albert Einstein College of Medicine, Bronx, NY 10461, United
     States.
AU   Glatman-Freedman, Aharona
CS   Department of Pediatrics, Division of Pediatric Infectious Diseases,
     Albert Einstein College of Medicine, Bronx, NY 1046, United States.
SO   Vaccine, (7 Nov 2007) Vol. 25, No. 45, pp. 7832-7840.
     Refs: 34
     ISSN: 0264-410X  CODEN: VACCDE
PUI  S 0264-410X(07)00965-6
CY   United Kingdom
DT   Journal; Article
FS   015     Chest Diseases, Thoracic Surgery and Tuberculosis
     026     Immunology, Serology and Transplantation
     037     Drug Literature Index
     004     Microbiology: Bacteriology, Mycology, Parasitology and Virology
LA   English
SL   English
ED   Entered STN: 7 Nov 2007
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Last Updated on STN: 7 Nov 2007

=> s e1-e4 and RD1 and auxotroph
L2 1 ("JACOBS JR W R JR"/AU OR "JACOBS JR WILLIAM"/AU OR "JACOBS JR WILLIAM R"/AU OR "JACOBS JR WILLIAM R JR"/AU) AND RD1 AND AUXOTROPH

=> d

L2 ANSWER 1 OF 1 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights reserved on STN
AN 2007506752 EMBASE <<LOGINID::20091103>>
TI Failure of a Mycobacterium tuberculosis .DELTA. ***RD1*** .DELTA.panCD double deletion mutant in a neonatal calf aerosol M. bovis challenge model: Comparisons to responses elicited by M. bovis bacille Calmette Guerin.
AU Waters, W. Ray (correspondence); Palmer, Mitchell V.; Nonnecke, Brian J.; Thacker, Tyler C.
CS National Animal Disease Center, Agricultural Research Service, US Department of Agriculture, 2300 Dayton Avenue, Ames, IA 50010, United States. ray.waters@ars.usda.gov
AU Scherer, Charles F. Capinos; Estes, D. Mark
CS University of Texas Medical Branch, Department of Pediatrics, the Sealy Center for Vaccine Development, Galveston, TX 77555, United States.
AU ***Jacobs Jr., William R.*** ; Larsen, Michelle H.
CS Howard Hughes Medical Institute, Department of Microbiology and Immunology, Albert Einstein College of Medicine, Bronx, NY 10461, United States.
AU Glatman-Freedman, Aharona
CS Department of Pediatrics, Division of Pediatric Infectious Diseases, Albert Einstein College of Medicine, Bronx, NY 1046, United States.
SO Vaccine, (7 Nov 2007) Vol. 25, No. 45, pp. 7832-7840.
Refs: 34
ISSN: 0264-410X CODEN: VACCDE
PUI S 0264-410X(07)00965-6
CY United Kingdom
DT Journal; Article
FS 015 Chest Diseases, Thoracic Surgery and Tuberculosis
026 Immunology, Serology and Transplantation
037 Drug Literature Index
004 Microbiology: Bacteriology, Mycology, Parasitology and Virology
LA English
SL English
ED Entered STN: 7 Nov 2007
Last Updated on STN: 7 Nov 2007

=> s e1-e4 and auxotroph and pantothenate
L3 4 ("JACOBS JR W R JR"/AU OR "JACOBS JR WILLIAM"/AU OR "JACOBS JR WILLIAM R"/AU OR "JACOBS JR WILLIAM R JR"/AU) AND AUXOTROPH AND PANTOTHENATE

=> dup rem l3
PROCESSING COMPLETED FOR L3
L4 4 DUP REM L3 (0 DUPLICATES REMOVED)

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YOU HAVE REQUESTED DATA FROM 4 ANSWERS - CONTINUE? Y/(N):y

L4   ANSWER 1 OF 4  EMBASE  COPYRIGHT (c) 2009 Elsevier B.V. All rights
     reserved on STN
AN   2007506752  EMBASE   <<LOGINID::20091103>>
TI   Failure of a Mycobacterium tuberculosis .DELTA.RD1 .DELTA.panCD double
     deletion mutant in a neonatal calf aerosol M. bovis challenge model:
     Comparisons to responses elicited by M. bovis bacille Calmette Guerin.
AU   Waters, W. Ray (correspondence); Palmer, Mitchell V.; Nonnecke, Brian J.;
     Thacker, Tyler C.
CS   National Animal Disease Center, Agricultural Research Service, US
     Department of Agriculture, 2300 Dayton Avenue, Ames, IA 50010, United
     States. ray.waters@ars.usda.gov
AU   Scherer, Charles F. Capinos; Estes, D. Mark
CS   University of Texas Medical Branch, Department of Pediatrics, the Sealy
     Center for Vaccine Development, Galveston, TX 77555, United States.
AU     ***Jacobs Jr., William R.***  ; Larsen, Michelle H.
CS   Howard Hughes Medical Institute, Department of Microbiology and
     Immunology, Albert Einstein College of Medicine, Bronx, NY 10461, United
     States.
AU   Glatman-Freedman, Aharona
CS   Department of Pediatrics, Division of Pediatric Infectious Diseases,
     Albert Einstein College of Medicine, Bronx, NY 1046, United States.
SO   Vaccine, (7 Nov 2007) Vol. 25, No. 45, pp. 7832-7840.
     Refs: 34
     ISSN: 0264-410X  CODEN: VACCDE
PUI  S 0264-410X(07)00965-6
CY   United Kingdom
DT   Journal; Article
FS   015     Chest Diseases, Thoracic Surgery and Tuberculosis
     026     Immunology, Serology and Transplantation
     037     Drug Literature Index
     004     Microbiology: Bacteriology, Mycology, Parasitology and Virology
LA   English
SL   English
ED   Entered STN: 7 Nov 2007
     Last Updated on STN: 7 Nov 2007

L4   ANSWER 2 OF 4  EMBASE  COPYRIGHT (c) 2009 Elsevier B.V. All rights
     reserved on STN
AN   2005054494  EMBASE   <<LOGINID::20091103>>
TI   Long-term protection against tuberculosis following vaccination with a
     severely attenuated double lysine and   ***pantothenate***
       ***auxotroph***   of Mycobacterium tuberculosis.
AU   Sambandamurthy, Vasan K.; Chen, Bing;   ***Jacobs Jr., William R.***
  ***     (correspondence)***
CS   Howard Hughes Medical Institute, Albert Einstein College of Medicine,
     Bronx, NY, United States. jacobsw@hhmi.org
AU   Sambandamurthy, Vasan K.; Jalapathy, Kripa V.; Chen, Bing;   ***Jacobs***
  ***     Jr., William R. (correspondence)***
CS   Dept. of Microbiology and Immunology, Albert Einstein College of Medicine,
     Bronx, NY, United States. jacobsw@hhmi.org
AU   Russell, Robert G.
CS   Department of Pathology, Lombardi Cancer Center, Georgetown University,
     Washington, DC, United States.
AU   Derrick, Steven C.; Morris, Sheldon L.
```

CS Ctr. for Biologics Eval. and Res., Food and Drug Administration, Bethesda, MD, United States.
AU ***Jacobs Jr., William R. (correspondence)***
CS Albert Einstein College of Medicine, 1300 Morris Park Ave., Bronx, NY 10461, United States. jacobsw@hhmi.org
SO Infection and Immunity, (Feb 2005) Vol. 73, No. 2, pp. 1196-1203.
Refs: 43
ISSN: 0019-9567 CODEN: INFIBR
CY United States
DT Journal; Article
FS 026 Immunology, Serology and Transplantation
037 Drug Literature Index
004 Microbiology: Bacteriology, Mycology, Parasitology and Virology
LA English
SL English
ED Entered STN: 18 Feb 2005
Last Updated on STN: 18 Feb 2005

L4 ANSWER 3 OF 4 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights reserved on STN
AN 2004188799 EMBASE <<LOGINID::20091103>>
TI Protection Elicited by a Double Leucine and ***Pantothenate*** ***Auxotroph*** of Mycobacterium tuberculosis in Guinea Pigs.
AU Sampson, Samantha L.; Bloom, Barry R.; Hondalus, Mary K. (correspondence)
CS Dept. of Immunol. and Infect. Dis., Harvard School of Public Health, 665 Huntington Ave., Boston, MA 02115, United States. mhondalu@hsph.harvard.edu
AU Dascher, Christopher C.
CS Brigham and Women's Hospital, Harvard Medical School, Boston, MA 02115, United States.
AU Sambandamurthy, Vasan K.; ***Jacobs Jr., William R.***
CS Albert Einstein College of Medicine, Bronx, NY 104613, United States.
AU Russell, Robert G.
CS Department of Pathology, Lombardi Cancer Center, Georgetown University, Washington, DC 20057, United States.
SO Infection and Immunity, (May 2004) Vol. 72, No. 5, pp. 3031-3037.
Refs: 33
ISSN: 0019-9567 CODEN: INFIBR
CY United States
DT Journal; Article
FS 015 Chest Diseases, Thoracic Surgery and Tuberculosis
026 Immunology, Serology and Transplantation
037 Drug Literature Index
004 Microbiology: Bacteriology, Mycology, Parasitology and Virology
LA English
SL English
ED Entered STN: 28 May 2004
Last Updated on STN: 28 May 2004

L4 ANSWER 4 OF 4 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights reserved on STN
AN 2002369070 EMBASE <<LOGINID::20091103>>
TI A ***pantothenate*** ***auxotroph*** of Mycobacterium tuberculosis is highly attenuated and protects mice against tuberculosis.
AU Sambandamurthy, Vasan K.; Wang, Xiaojuan; Chen, Bing; Russell, Robert G.; Derrick, Steven; Collins, Frank M.; Morris, Sheldon L.; ***Jacobs Jr.,*** ***William R. (correspondence)***

CS Howard Hughes Medical Institute, Department of Microbiology, Albert Einstein College of Medicine, Bronx, NY, United States. jacobsw@hhmi.org
SO Nature Medicine, (1 Oct 2002) Vol. 8, No. 10, pp. 1171-1174.
Refs: 23
ISSN: 1078-8956 CODEN: NAMEFI
CY United States
DT Journal; Article
FS 015 Chest Diseases, Thoracic Surgery and Tuberculosis
026 Immunology, Serology and Transplantation
030 Clinical and Experimental Pharmacology
037 Drug Literature Index
004 Microbiology: Bacteriology, Mycology, Parasitology and Virology
LA English
SL English
ED Entered STN: 7 Nov 2002
Last Updated on STN: 7 Nov 2002

=> s l4 and ?panCD
LEFT TRUNCATION IGNORED FOR FILE 'LIFESCI'
L5 3 L4 AND ?PANCD
=> d bib ab kwic 1-
YOU HAVE REQUESTED DATA FROM 3 ANSWERS - CONTINUE? Y/(N):y

L5 ANSWER 1 OF 3 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights reserved on STN
AN 2007506752 EMBASE <<LOGINID::20091103>>
TI Failure of a Mycobacterium tuberculosis .DELTA.RD1 .DELTA. ***panCD*** double deletion mutant in a neonatal calf aerosol M. bovis challenge model: Comparisons to responses elicited by M. bovis bacille Calmette Guerin.
AU Waters, W. Ray (correspondence); Palmer, Mitchell V.; Nonnecke, Brian J.; Thacker, Tyler C.
CS National Animal Disease Center, Agricultural Research Service, US Department of Agriculture, 2300 Dayton Avenue, Ames, IA 50010, United States. ray.waters@ars.usda.gov
AU Scherer, Charles F. Capinos; Estes, D. Mark
CS University of Texas Medical Branch, Department of Pediatrics, the Sealy Center for Vaccine Development, Galveston, TX 77555, United States.
AU ***Jacobs Jr., William R.*** ; Larsen, Michelle H.
CS Howard Hughes Medical Institute, Department of Microbiology and Immunology, Albert Einstein College of Medicine, Bronx, NY 10461, United States.
AU Glatman-Freedman, Aharona
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SO Vaccine, (7 Nov 2007) Vol. 25, No. 45, pp. 7832-7840.
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ISSN: 0264-410X CODEN: VACCDE
PUI S 0264-410X(07)00965-6
CY United Kingdom
DT Journal; Article
FS 015 Chest Diseases, Thoracic Surgery and Tuberculosis
026 Immunology, Serology and Transplantation
037 Drug Literature Index
004 Microbiology: Bacteriology, Mycology, Parasitology and Virology
LA English

SL English
ED Entered STN: 7 Nov 2007
Last Updated on STN: 7 Nov 2007
AB An attenuated Mycobacterium tuberculosis RD1 knockout and ***pantothenate*** ***auxotroph*** (mc26030) vaccine administered at 2 weeks of age failed to protect calves from low dose, aerosol M. bovis challenge at 2.5 months of age. In contrast, M. bovis bacille Calmette Guerin (BCG)-vaccinates had reduced tuberculosis-associated pathology as compared to non- and mc26030-vaccinates. Mycobacterial colonization was not impacted by vaccination. Positive prognostic indicators associated with reduced pathology in the BCG-vaccinated group were decreased antigen induced IFN-.gamma., iNOS, IL-4, and MIP1-.alpha. responses, increased antigen induced FoxP3 expression, and a diminished activation phenotype (i.e., .dwnarw.CD25+ and CD44+ cells and .uparw.CD62L+ cells) in mycobacterial-stimulated mononuclear cell cultures. The calf sensitization and challenge model provides an informative screen for candidate tuberculosis vaccines before their evaluation in costly non-human, primates.
TI Failure of a Mycobacterium tuberculosis .DELTA.RD1 .DELTA. ***panCD*** double deletion mutant in a neonatal calf aerosol M. bovis challenge model: Comparisons to responses elicited by M. bovis bacille. . .
AU ***Jacobs Jr., William R.*** ; Larsen, Michelle H.
CS Howard Hughes Medical Institute, Department of Microbiology and Immunology, Albert Einstein College of. . .
AB An attenuated Mycobacterium tuberculosis RD1 knockout and ***pantothenate*** ***auxotroph*** (mc26030) vaccine administered at 2 weeks of age failed to protect calves from low dose, aerosol M. bovis challenge at. . .

L5 ANSWER 2 OF 3 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights reserved on STN
AN 2005054494 EMBASE <<LOGINID::20091103>>
TI Long-term protection against tuberculosis following vaccination with a severely attenuated double lysine and ***pantothenate*** ***auxotroph*** of Mycobacterium tuberculosis.
AU Sambandamurthy, Vasan K.; Chen, Bing; ***Jacobs Jr., William R.*** ***** (correspondence)***
CS Howard Hughes Medical Institute, Albert Einstein College of Medicine, Bronx, NY, United States. jacobsw@hhmi.org
AU Sambandamurthy, Vasan K.; Jalapathy, Kripa V.; Chen, Bing; ***Jacobs*** ***** Jr., William R. (correspondence)***
CS Dept. of Microbiology and Immunology, Albert Einstein College of Medicine, Bronx, NY, United States. jacobsw@hhmi.org
AU Russell, Robert G.
CS Department of Pathology, Lombardi Cancer Center, Georgetown University, Washington, DC, United States.
AU Derrick, Steven C.; Morris, Sheldon L.
CS Ctr. for Biologics Eval. and Res., Food and Drug Administration, Bethesda, MD, United States.
AU ***Jacobs Jr., William R. (correspondence)***
CS Albert Einstein College of Medicine, 1300 Morris Park Ave., Bronx, NY 10461, United States. jacobsw@hhmi.org
SO Infection and Immunity, (Feb 2005) Vol. 73, No. 2, pp. 1196-1203.
Refs: 43
ISSN: 0019-9567 CODEN: INFIBR

CY United States
DT Journal; Article
FS 026 Immunology, Serology and Transplantation
037 Drug Literature Index
004 Microbiology: Bacteriology, Mycology, Parasitology and Virology
LA English
SL English
ED Entered STN: 18 Feb 2005
Last Updated on STN: 18 Feb 2005
AB We report the safety and immunogenicity of a double lysine and ***pantothenate*** ***auxotroph*** of Mycobacterium tuberculosis in mice. The .DELTA.lysA .DELTA. ***panCD*** mutant is completely attenuated in immunocompromised SCID and gamma interferon knockout mice yet induces short-term and long-term protection in immunocompetent and CD4-deficient mice following single-dose subcutaneous vaccination.
TI Long-term protection against tuberculosis following vaccination with a severely attenuated double lysine and ***pantothenate*** ***auxotroph*** of Mycobacterium tuberculosis.
AU Sambandamurthy, Vasan K.; Chen, Bing; ***Jacobs Jr., William R.*** *** (correspondence)***
CS Howard Hughes Medical Institute, Albert Einstein College of Medicine, Bronx, NY, United States. jacobsw@hhmi.org
AU Sambandamurthy, Vasan K.; Jalapathy, Kripa V.; Chen, Bing; ***Jacobs*** *** Jr., William R. (correspondence)***
CS Dept. of Microbiology and Immunology, Albert Einstein College of Medicine, Bronx, NY, United States.. . .
AU ***Jacobs Jr., William R. (correspondence)***
CS Albert Einstein College of Medicine, 1300 Morris Park Ave., Bronx, NY 10461, United States.. . .
AB We report the safety and immunogenicity of a double lysine and ***pantothenate*** ***auxotroph*** of Mycobacterium tuberculosis in mice. The .DELTA.lysA .DELTA. ***panCD*** mutant is completely attenuated in immunocompromised SCID and gamma interferon knockout mice yet induces short-term and long-term protection in immunocompetent. . .
CT Medical Descriptors:
animal . . . safety
immune deficiency
immunocompetence
infection prevention
knockout mouse
mouse
*Mycobacterium tuberculosis
nonhuman
priority journal
SCID mouse
*tuberculosis
*BCG vaccine: DV, drug development
*BCG vaccine: DO, drug dose
*BCG vaccine: SC, subcutaneous drug administration
****double lysine pantothenate mycobacterium tuberculosis vaccine: DV,***
*** drug development***
****double lysine pantothenate mycobacterium tuberculosis vaccine: DO,***
*** drug dose***
****double lysine pantothenate mycobacterium tuberculosis vaccine: SC,***

*** subcutaneous drug administration***
gamma interferon
*live vaccine: DV, drug development
*live vaccine: DO, drug dose
*live vaccine: SC,. . .

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AN 2004188799 EMBASE <<LOGINID::20091103>>
TI Protection Elicited by a Double Leucine and ***Pantothenate*** ***Auxotroph*** of Mycobacterium tuberculosis in Guinea Pigs.
AU Sampson, Samantha L.; Bloom, Barry R.; Hondalus, Mary K. (correspondence)
CS Dept. of Immunol. and Infect. Dis., Harvard School of Public Health, 665 Huntington Ave., Boston, MA 02115, United States. mhondalu@hsph.harvard.edu
AU Dascher, Christopher C.
CS Brigham and Women's Hospital, Harvard Medical School, Boston, MA 02115, United States.
AU Sambandamurthy, Vasan K.; ***Jacobs Jr., William R.***
CS Albert Einstein College of Medicine, Bronx, NY 104613, United States.
AU Russell, Robert G.
CS Department of Pathology, Lombardi Cancer Center, Georgetown University, Washington, DC 20057, United States.
SO Infection and Immunity, (May 2004) Vol. 72, No. 5, pp. 3031-3037.
Refs: 33
ISSN: 0019-9567 CODEN: INFIBR
CY United States
DT Journal; Article
FS 015 Chest Diseases, Thoracic Surgery and Tuberculosis
026 Immunology, Serology and Transplantation
037 Drug Literature Index
004 Microbiology: Bacteriology, Mycology, Parasitology and Virology
LA English
SL English
ED Entered STN: 28 May 2004
Last Updated on STN: 28 May 2004
AB We developed a live, fully attenuated Mycobacterium tuberculosis vaccine candidate strain with two independent attenuating auxotrophic mutations in leucine and ***pantothenate*** biosynthesis. The .DELTA.leuD .DELTA. ***panCD*** double ***auxotroph*** is fully attenuated in the SCID mouse model and highly immunogenic and protective in the extremely sensitive guinea pig tuberculosis model, reducing both bacterial burden and disease pathology.
TI Protection Elicited by a Double Leucine and ***Pantothenate*** ***Auxotroph*** of Mycobacterium tuberculosis in Guinea Pigs.
AU Sambandamurthy, Vasan K.; ***Jacobs Jr., William R.***
CS Albert Einstein College of Medicine, Bronx, NY 104613, United States.
AB . . . We developed a live, fully attenuated Mycobacterium tuberculosis vaccine candidate strain with two independent attenuating auxotrophic mutations in leucine and ***pantothenate*** biosynthesis. The .DELTA.leuD .DELTA. ***panCD*** double ***auxotroph*** is fully attenuated in the SCID mouse model and highly immunogenic and protective in the extremely sensitive guinea pig tuberculosis. . .

=> e hsu tsungda/au
E1 18 HSU TSUNG YUAN/AU

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E2            1     HSU TSUNG YUEH/AU
E3           97 --> HSU TSUNGDA/AU
E4            1     HSU TSUNGJEN/AU
E5            1     HSU TSUNGWEN/AU
E6            1     HSU TSUNGYANG/AU
E7            3     HSU TSWEI FUNG/AU
E8           21     HSU TSZ CHING/AU
E9            1     HSU TSZ CHING DR/AU
E10           4     HSU TUAN CHENG/AU
E11           6     HSU TUAN FU/AU
E12           1     HSU TUAN JUNG/AU

=> s e3 and auxotroph and pantothenate
L6            2 "HSU TSUNGDA"/AU AND AUXOTROPH AND PANTOTHENATE

=> dup rem l6
PROCESSING COMPLETED FOR L6
L7             2 DUP REM L6 (0 DUPLICATES REMOVED)

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YOU HAVE REQUESTED DATA FROM 2 ANSWERS - CONTINUE? Y/(N):y

L7   ANSWER 1 OF 2  SCISEARCH  COPYRIGHT (c) 2009 The Thomson Corporation  on
     STN
AN   2009:930391  SCISEARCH <<LOGINID::20091103>>
GA   The Genuine Article (R) Number: 475IG
TI   Efficacy and safety of live attenuated persistent and rapidly cleared
     Mycobacterium tuberculosis vaccine candidates in non-human primates
AU   Larsen, Michelle H. (Reprint)
CS   Albert Einstein Coll Med, 1301 Morris Pk Ave, Bronx, NY 10467 USA
     (Reprint)
     E-mail: larsen@aecom.yu.edu
AU   Larsen, Michelle H. (Reprint); Biermann, Karolin; Chen, Bing;   ***Hsu,***
  ***     Tsungda***  ; Jacobs, William R., Jr.
CS   Albert Einstein Coll Med, Bronx, NY 10467 USA
     E-mail: larsen@aecom.yu.edu
AU   Sambandamurthy, Vasan K.
CS   AstraZeneca, Bangalore, Karnataka, India
AU   Lackner, Andrew A.; Aye, Pyone Pyone; Didier, Peter
CS   Tulane Natl Primate Res Ctr, Covington, LA 70433 USA
AU   Huang, Dan; Shao, Linyun; Wei, Huiyong; Chen, Zheng W.
CS   Univ Illinois, Coll Med, Chicago, IL USA
AU   Huang, Dan; Shao, Linyun; Wei, Huiyong; Chen, Zheng W.
CS   Ctr Primate Biomed Res, Dept Microbiol & Immunol, Chicago, IL 60612 USA
AU   Letvin, Norman L.
CS   Harvard Univ, Beth Israel Deaconess Med Ctr, Sch Med, Boston, MA 02215 USA
AU   Frothingham, Richard; Haynes, Barton F.
CS   Duke Univ, Duke Human Vaccine Inst, Durham, NC 27710 USA
CYA  USA; India
SO   VACCINE, (23 JUL 2009) Vol. 27, No. 34, pp. 4709-4717.
     ISSN: 0264-410X.
PB   ELSEVIER SCI LTD, THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD OX5
     1GB, OXON, ENGLAND.
DT   Article; Journal
LA   English
REC  Reference Count: 29
ED   Entered STN: 6 Aug 2009
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     Last Updated on STN: 6 Aug 2009
     *ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*

L7   ANSWER 2 OF 2  SCISEARCH  COPYRIGHT (c) 2009 The Thomson Corporation  on
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AN   2007:108973  SCISEARCH <<LOGINID::20091103>>
GA   The Genuine Article (R) Number: 122PP
TI   Characterization of the protective T-cell response generated in
     CD4-deficient mice by a live attenuated Mycobacterium tuberculosis vaccine
AU   Derrick, Steven C. (Reprint)
CS   NINCDS, Ctr Biol Evaluat & Res, Bldg 10, Bethesda, MD 20892 USA (Reprint)
AU   Evering, Teresa H.; Sambandamurthy, Vasan K.; Jalapathy, Kripa V.;
       ***Hsu, Tsungda***  ; Chen, Bing; Chen, Mei; Russell, Robert G.;
     Junqueira-Kipnis, Ana Paula; Orme, Ian M.; Porcelli, Steven A.; Jacobs,
     William R., Jr.; Morris, Sheldon L.
CS   NINCDS, Ctr Biol Evaluat & Res, Bethesda, MD 20892 USA; Albert Einstein
     Coll Med, Dept Microbiol & Immunol, Bronx, NY 10467 USA; Howard Hughes Med
     Inst, Chevy Chase, MD USA; Georgetown Univ, Lombardi Canc Ctr, Dept
     Pathol, Washington, DC 20007 USA; Colorado State Univ, Dept Microbiol
     Immunol & Pathol, Ft Collins, CO 80523 USA
     E-mail: steven.derrick@fda.hhs.gov; Jacobsw@hhmi.org
CYA  USA
SO   IMMUNOLOGY, (FEB 2007) Vol. 120, No. 2, pp. 192-206.
     ISSN: 0019-2805.
PB   BLACKWELL PUBLISHING, 9600 GARSINGTON RD, OXFORD OX4 2DQ, OXON, ENGLAND.
DT   Article; Journal
LA   English
REC  Reference Count: 48
ED   Entered STN: 1 Feb 2007
     Last Updated on STN: 1 Feb 2007
     *ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*


=> e sambandamurthy vasan/au
E1            2     SAMBANDAMURTHY V/AU
E2           12     SAMBANDAMURTHY V K/AU
E3            7 --> SAMBANDAMURTHY VASAN/AU
E4           48     SAMBANDAMURTHY VASAN K/AU
E5            6     SAMBANDAN A/AU
E6            2     SAMBANDAN ARIVAZHAGAN/AU
E7            1     SAMBANDAN D R/AU
E8           13     SAMBANDAN DEEPA/AU
E9            6     SAMBANDAN DHINAKARAN/AU
E10          11     SAMBANDAN DIVYA R/AU
E11           5     SAMBANDAN G/AU
E12          24     SAMBANDAN K/AU

=> s e1-e4 and auxotroph and pantothenate
L8           22 ("SAMBANDAMURTHY V"/AU OR "SAMBANDAMURTHY V K"/AU OR "SAMBANDAMU
                RTHY VASAN"/AU OR "SAMBANDAMURTHY VASAN K"/AU) AND AUXOTROPH
                AND PANTOTHENATE

=> dup rem l8
PROCESSING COMPLETED FOR L8
L9             7 DUP REM L8 (15 DUPLICATES REMOVED)

=> s l9 and panCD
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L10 3 L9 AND PANCD

=> d bib ab kwic 1-
YOU HAVE REQUESTED DATA FROM 3 ANSWERS - CONTINUE? Y/(N):y

L10 ANSWER 1 OF 3 SCISEARCH COPYRIGHT (c) 2009 The Thomson Corporation on STN
AN 2009:930391 SCISEARCH <<LOGINID::20091103>>
GA The Genuine Article (R) Number: 475IG
TI Efficacy and safety of live attenuated persistent and rapidly cleared Mycobacterium tuberculosis vaccine candidates in non-human primates
AU Larsen, Michelle H. (Reprint)
CS Albert Einstein Coll Med, 1301 Morris Pk Ave, Bronx, NY 10467 USA (Reprint)
E-mail: larsen@aecom.yu.edu
AU Larsen, Michelle H. (Reprint); Biermann, Karolin; Chen, Bing; Hsu, Tsungda; Jacobs, William R., Jr.
CS Albert Einstein Coll Med, Bronx, NY 10467 USA
E-mail: larsen@aecom.yu.edu
AU ***Sambandamurthy, Vasan K.***
CS AstraZeneca, Bangalore, Karnataka, India
AU Lackner, Andrew A.; Aye, Pyone Pyone; Didier, Peter
CS Tulane Natl Primate Res Ctr, Covington, LA 70433 USA
AU Huang, Dan; Shao, Linyun; Wei, Huiyong; Chen, Zheng W.
CS Univ Illinois, Coll Med, Chicago, IL USA
AU Huang, Dan; Shao, Linyun; Wei, Huiyong; Chen, Zheng W.
CS Ctr Primate Biomed Res, Dept Microbiol & Immunol, Chicago, IL 60612 USA
AU Letvin, Norman L.
CS Harvard Univ, Beth Israel Deaconess Med Ctr, Sch Med, Boston, MA 02215 USA
AU Frothingham, Richard; Haynes, Barton F.
CS Duke Univ, Duke Human Vaccine Inst, Durham, NC 27710 USA
CYA USA; India
SO VACCINE, (23 JUL 2009) Vol. 27, No. 34, pp. 4709-4717.
ISSN: 0264-410X.
PB ELSEVIER SCI LTD, THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD OX5 1GB, OXON, ENGLAND.
DT Article; Journal
LA English
REC Reference Count: 29
ED Entered STN: 6 Aug 2009
Last Updated on STN: 6 Aug 2009
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Tuberculosis (TB) remains a global health burden for which safe vaccines are needed. BCG has limitations as a TB vaccine so we have focused on live attenuated Mycobacterium tuberculosis mutants as vaccine candidates. Prior to human studies, however, it is necessary to demonstrate safety in non-human primates (NHP). In this study, we evaluate the safety and efficacy of two live attenuated M. tuberculosis double deletion vaccine strains mc(2)6020 (Delta lysA Delta ***panCD***) and mc(2)6030 (Delta RD1 Delta ***panCD***) in cynomolgus macaques. In murine models, mc(2)6020 is rapidly cleared while mc(2)6030 persists. Both mc(2)6020 and mc(2)6030 were safe and well tolerated in cynomolgus macaques. Following a high-dose intrabronchial challenge with virulent M. tuberculosis, mc(2)6020-vaccinates were afforded a level of protection intermediate between that elicited by BCG vaccination and no vaccination. BCG vaccinates had reduced tuberculosis-associated pathology and improved clinical scores as compared to saline and mc(2)6030 vaccinates, but

survival did not differ among the groups. (C) 2009 Elsevier Ltd. All rights reserved.
AU ***Sambandamurthy, Vasan K.***
CS AstraZeneca, Bangalore, Karnataka, India
AB . . . we evaluate the safety and efficacy of two live attenuated M. tuberculosis double deletion vaccine strains mc(2)6020 (Delta lysA Delta ***panCD***) and mc(2)6030 (Delta RD1 Delta ***panCD***) in cynomolgus macaques. In murine models, mc(2)6020 is rapidly cleared while mc(2)6030 persists. Both mc(2)6020 and mc(2)6030 were safe and. . .
STP KeyWords Plus (R): BACILLE-CALMETTE-GUERIN; DELTA-RD1 DELTA- ***PANCD*** ; T-CELL RESPONSES; ***PANTOTHENATE*** ***AUXOTROPH*** ; CYNOMOLGUS MONKEY; BCG VACCINATION; INFECTION; PROTECTION; MACAQUES; MODEL

L10 ANSWER 2 OF 3 SCISEARCH COPYRIGHT (c) 2009 The Thomson Corporation on STN
AN 2007:108973 SCISEARCH <<LOGINID::20091103>>
GA The Genuine Article (R) Number: 122PP
TI Characterization of the protective T-cell response generated in CD4-deficient mice by a live attenuated Mycobacterium tuberculosis vaccine
AU Derrick, Steven C. (Reprint)
CS NINCDS, Ctr Biol Evaluat & Res, Bldg 10, Bethesda, MD 20892 USA (Reprint)
AU Evering, Teresa H.; ***Sambandamurthy, Vasan K.*** ; Jalapathy, Kripa V.; Hsu, Tsungda; Chen, Bing; Chen, Mei; Russell, Robert G.; Junqueira-Kipnis, Ana Paula; Orme, Ian M.; Porcelli, Steven A.; Jacobs, William R., Jr.; Morris, Sheldon L.
CS NINCDS, Ctr Biol Evaluat & Res, Bethesda, MD 20892 USA; Albert Einstein Coll Med, Dept Microbiol & Immunol, Bronx, NY 10467 USA; Howard Hughes Med Inst, Chevy Chase, MD USA; Georgetown Univ, Lombardi Canc Ctr, Dept Pathol, Washington, DC 20007 USA; Colorado State Univ, Dept Microbiol Immunol & Pathol, Ft Collins, CO 80523 USA
E-mail: steven.derrick@fda.hhs.gov; Jacobsw@hhmi.org
CYA USA
SO IMMUNOLOGY, (FEB 2007) Vol. 120, No. 2, pp. 192-206.
ISSN: 0019-2805.
PB BLACKWELL PUBLISHING, 9600 GARSINGTON RD, OXFORD OX4 2DQ, OXON, ENGLAND.
DT Article; Journal
LA English
REC Reference Count: 48
ED Entered STN: 1 Feb 2007
Last Updated on STN: 1 Feb 2007
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB The global epidemic of tuberculosis, fuelled by acquired immune-deficiency syndrome, necessitates the development of a safe and effective vaccine. We have constructed a Delta RD1 Delta ***panCD*** mutant of Mycobacterium tuberculosis (mc(2)6030) that undergoes limited replication and is severely attenuated in immunocompromised mice, yet induces significant protection against tuberculosis in wild-type mice and even in mice that completely lack CD4(+) T cells as a result of targeted disruption of their CD4 genes (CD4(-/-) mice). Ex vivo studies of T cells from mc(2)6030-immunized mice showed that these immune cells responded to protein antigens of M. tuberculosis in a major histocompatibility complex (MHC) class II-restricted manner. Antibody depletion experiments showed that antituberculosis protective responses in the lung were not diminished by removal of CD8(+), T-cell receptor gamma delta (TCR-gamma delta(+)) and NK1.1(+) T cells from vaccinated CD4(-/-) mice before challenge, implying that the observed recall and immune effector functions resulting from vaccination of CD4(-/-) mice with mc(2)6030 were attributable to a

population of CD4(-) CD8(-) (double-negative) TCR-alpha beta(+), TCR-gamma delta(-), NK1.1(-) T cells. Transfer of highly enriched double-negative TCR-alpha beta(+) T cells from mc(2)6030-immunized CD4(-/-) mice into naive CD4(-/-) mice resulted in significant protection against an aerosol tuberculosis challenge. Enriched pulmonary double-negative T cells transcribed significantly more interferon-gamma and interleukin-2 mRNA than double-negative T cells from naive mice after a tuberculous challenge. These results confirmed previous findings on the potential for a subset of MHC class II-restricted T cells to develop and function without expression of CD4 and suggest novel vaccination strategies to assist in the control of tuberculosis in human immunodeficiency virus-infected humans who have chronic depletion of their CD4(+) T cells.

AU Evering, Teresa H.; ***Sambandamurthy, Vasan K.*** ; Jalapathy, Kripa V.; Hsu, Tsungda; Chen, Bing; Chen, Mei; Russell, Robert G.; Junqueira-Kipnis, Ana Paula; Orme, Ian M.;. . .

AB . . . by acquired immune-deficiency syndrome, necessitates the development of a safe and effective vaccine. We have constructed a Delta RD1 Delta ***panCD*** mutant of Mycobacterium tuberculosis (mc(2)6030) that undergoes limited replication and is severely attenuated in immunocompromised mice, yet induces significant protection. . .

STP KeyWords Plus (R): INTRACELLULARE COMPLEX INFECTION; ***PANTOTHENATE*** ***AUXOTROPH*** ; PULMONARY TUBERCULOSIS; ANTIGEN PRESENTATION; CD8-T-CELL MEMORY; CD4-T-CELL HELP; CALMETTE-GUERIN; BOVIS BCG; CD4; LYMPHOCYTES

L10 ANSWER 3 OF 3 SCISEARCH COPYRIGHT (c) 2009 The Thomson Corporation on STN

AN 2006:955923 SCISEARCH <<LOGINID::20091103>>

GA The Genuine Article (R) Number: 086VX

TI Mycobacterium tuberculosis Delta RD1 Delta ***panCD*** : A safe and limited replicating mutant strain that protects immunocompetent and immunocompromised mice against experimental tuberculosis

AU ***Sambandamurthy V K (Reprint)*** ; Derrick S C; Hsu T; Chen B; Larsen M H; Jalapathy K V; Chen M; Kim J; Porcelli S A; Chan J; Morris S L; Jacobs W R

CS US FDA, Ctr Biol Evaluat & Res, Bethesda, MD 20892 USA; Albert Einstein Coll Med, Dept Microbiol & Immunol, Bronx, NY 10461 USA; Albert Einstein Coll Med, Dept Med, Bronx, NY 10461 USA; Novartis Inst Trop Dis, Singapore 138670, Singapore
E-mail: jacobsw@hhmi.org

CYA USA; Singapore

SO VACCINE, (11 SEP 2006) Vol. 24, No. 37-39, pp. 6309-6320.
ISSN: 0264-410X.

PB ELSEVIER SCI LTD, THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD OX5 1GB, OXON, ENGLAND.

DT Article; Journal

LA English

REC Reference Count: 40

ED Entered STN: 18 Oct 2006
Last Updated on STN: 18 Oct 2006

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The global epidemic of tuberculosis (TB), fueled by the growing HIV pandemic, warrants the development of a safe and effective vaccine against TB. We report the construction and characterization of an unlinked double deletion mutant of Mycobacterium tuberculosis H37Rv that deletes both the primary attenuating mutation of BCG (Delta RD1) and two genes required for the synthesis of ***pantothenate*** (Delta ***panCD***). The M.

tuberculosis Delta RD1 Delta ***panCD*** (mc(2)6030) mutant undergoes limited replication in mice, and yet is both significantly safer than BCG in immunocompromised mice and also safe in guinea pigs. Additionally, the mc(2)6030 strain does not reactivate in a mouse chemo-immunosuppression model. Importantly, long-lived protective immune responses following immunization with the mc(2)6030 strain prolong the survival of wild type mice, and CD4-deficient mice against an aerosol challenge with virulent M. tuberculosis. Given its overall safety and effectiveness, the mc(2)6030 live attenuated strain should be considered as a human vaccine candidate for protecting both healthy and HIV-infected individuals against TB. (c) 2006 Elsevier Ltd. All rights reserved.

TI Mycobacterium tuberculosis Delta RD1 Delta ***panCD*** : A safe and limited replicating mutant strain that protects immunocompetent and immunocompromised mice against experimental tuberculosis

AU ***Sambandamurthy V K (Reprint)*** ; Derrick S C; Hsu T; Chen B; Larsen M H; Jalapathy K V; Chen M; Kim J;. . .

AB . . . H37Rv that deletes both the primary attenuating mutation of BCG (Delta RD1) and two genes required for the synthesis of ***pantothenate*** (Delta ***panCD***). The M. tuberculosis Delta RD1 Delta ***panCD*** (mc(2)6030) mutant undergoes limited replication in mice, and yet is both significantly safer than BCG in immunocompromised mice and also. . .

STP KeyWords Plus (R): BACILLUS-CALMETTE-GUERIN; T-CELL SUBSETS; BOVIS BCG; ***PANTOTHENATE*** ***AUXOTROPH*** ; INTERFERON-GAMMA; IN-VITRO; IMMUNODEFICIENT MICE; IMMUNE-RESPONSE; INFECTION; VACCINES

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E2           2     MORRIS SHELBY J/AU
E3          47 --> MORRIS SHELDON/AU
E4           2     MORRIS SHELDON DR/AU
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E6           1     MORRIS SHELDON LEE/AU
E7          16     MORRIS SHELDON R/AU
E8           1     MORRIS SHELDON R DR/AU
E9           2     MORRIS SHELIA L/AU
E10         24     MORRIS SHELLI M/AU
E11          2     MORRIS SHERI/AU
E12          3     MORRIS SHERICCA/AU

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L11         12 ("MORRIS SHELDON"/AU OR "MORRIS SHELDON DR"/AU OR "MORRIS SHELDO
               N L"/AU OR "MORRIS SHELDON LEE"/AU OR "MORRIS SHELDON R"/AU OR
               "MORRIS SHELDON R DR"/AU) AND AUXOTROPH AND PANTOTHENATE

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PROCESSING COMPLETED FOR L11
L12           5 DUP REM L11 (7 DUPLICATES REMOVED)

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YOU HAVE REQUESTED DATA FROM 5 ANSWERS - CONTINUE? Y/(N):y

L12  ANSWER 1 OF 5  SCISEARCH  COPYRIGHT (c) 2009 The Thomson Corporation  on
     STN
AN   2007:1016623  SCISEARCH <<LOGINID::20091103>>
GA   The Genuine Article (R) Number: 196JS
TI   Enhanced priming of adaptive immunity by a proapoptotic mutant of
```

Mycobacterium tuberculosis
AU Jacobs, William R., Jr. (Reprint)
CS Yeshiva Univ Albert Einstein Coll Med, Howard Hughes Med Inst, 1300 Morris Pk Ave, Bronx, NY 10461 USA (Reprint)
AU Hinchey, Joseph; Lee, Sunhee; Jeon, Bo Y.; Basaraba, Randall J.; Venkataswamy, Manjunatha M.; Chen, Bing; Chan, John; Braunstein, Miriam; Orme, Ian M.; Derrick, Steven C.; ***Morris, Sheldon L.*** ; Porcelli, Steven A.
CS Yeshiva Univ Albert Einstein Coll Med, Howard Hughes Med Inst, Bronx, NY 10461 USA; Yeshiva Univ Albert Einstein Coll Med, Dept Microbiol & Immunol, Bronx, NY 10461 USA; US FDA, Ctr Biol Evaluat & Res, Bethesda, MD 20014 USA; Colorado State Univ, Dept Microbiol Immunol & Pathol, Ft Collins, CO 80523 USA; Albert Einstein Coll Med, Dept Med, New York, NY USA; Univ N Carolina, Dept Microbiol, Chapel Hill, NC USA
E-mail: jacobs@aecom.yu.edu; porcelli@aecom.yu.edu
CYA USA
SO JOURNAL OF CLINICAL INVESTIGATION, (AUG 2007) Vol. 117, No. 8, pp. 2279-2288.
ISSN: 0021-9738.
PB AMER SOC CLINICAL INVESTIGATION INC, 35 RESEARCH DR, STE 300, ANN ARBOR, MI 48103 USA.
DT Article; Journal
LA English
REC Reference Count: 47
ED Entered STN: 11 Oct 2007
Last Updated on STN: 11 Oct 2007
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

L12 ANSWER 2 OF 5 SCISEARCH COPYRIGHT (c) 2009 The Thomson Corporation on STN
AN 2007:108973 SCISEARCH <<LOGINID::20091103>>
GA The Genuine Article (R) Number: 122PP
TI Characterization of the protective T-cell response generated in CD4-deficient mice by a live attenuated Mycobacterium tuberculosis vaccine
AU Derrick, Steven C. (Reprint)
CS NINCDS, Ctr Biol Evaluat & Res, Bldg 10, Bethesda, MD 20892 USA (Reprint)
AU Evering, Teresa H.; Sambandamurthy, Vasan K.; Jalapathy, Kripa V.; Hsu, Tsungda; Chen, Bing; Chen, Mei; Russell, Robert G.; Junqueira-Kipnis, Ana Paula; Orme, Ian M.; Porcelli, Steven A.; Jacobs, William R., Jr.; ***Morris, Sheldon L.***
CS NINCDS, Ctr Biol Evaluat & Res, Bethesda, MD 20892 USA; Albert Einstein Coll Med, Dept Microbiol & Immunol, Bronx, NY 10467 USA; Howard Hughes Med Inst, Chevy Chase, MD USA; Georgetown Univ, Lombardi Canc Ctr, Dept Pathol, Washington, DC 20007 USA; Colorado State Univ, Dept Microbiol Immunol & Pathol, Ft Collins, CO 80523 USA
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CYA USA
SO IMMUNOLOGY, (FEB 2007) Vol. 120, No. 2, pp. 192-206.
ISSN: 0019-2805.
PB BLACKWELL PUBLISHING, 9600 GARSINGTON RD, OXFORD OX4 2DQ, OXON, ENGLAND.
DT Article; Journal
LA English
REC Reference Count: 48
ED Entered STN: 1 Feb 2007
Last Updated on STN: 1 Feb 2007
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

L12 ANSWER 3 OF 5 SCISEARCH COPYRIGHT (c) 2009 The Thomson Corporation on STN
AN 2006:1074555 SCISEARCH <<LOGINID::20091103>>
GA The Genuine Article (R) Number: 099NA
TI Protection elicited by two glutamine auxotrophs of Mycobacterium tuberculosis and in vivo growth phenotypes of the four unique glutamine synthetase mutants in a murine model
AU Jacobs, William R., Jr. (Reprint)
CS Albert Einstein Coll Med, Howard Hughes Med Inst, 1300 Morris Pk Ave, Bronx, NY 10461 USA (Reprint)
AU Lee, Sunhee; Jeon, Bo-Young; Bardarov, Svetoslav; Chen, Mei; ***Morris,*** *** Sheldon L.***
CS Albert Einstein Coll Med, Howard Hughes Med Inst, Bronx, NY 10461 USA; Albert Einstein Coll Med, Dept Microbiol & Immunol, Bronx, NY 10461 USA; US FDA, Ctr Biol Evaluat & Res, Bethesda, MD 20014 USA; Univ Massachusetts, Dept Pathol, Worcester, MA 01605 USA
E-mail: jacobsw@hhmi.org
CYA USA
SO INFECTION AND IMMUNITY, (NOV 2006) Vol. 74, No. 11, pp. 6491-6495.
ISSN: 0019-9567.
PB AMER SOC MICROBIOLOGY, 1752 N ST NW, WASHINGTON, DC 20036-2904 USA.
DT Article; Journal
LA English
REC Reference Count: 27
ED Entered STN: 16 Nov 2006
Last Updated on STN: 16 Nov 2006
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

L12 ANSWER 4 OF 5 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN DUPLICATE 1
AN 2005:169360 BIOSIS <<LOGINID::20091103>>
DN PREV200500170314
TI Long-term protection against tuberculosis following vaccination with a severely attenuated double lysine and ***pantothenate*** ***auxotroph*** of Mycobacterium tuberculosis.
AU Sambandamurthy, Vasan K.; Derrick, Steven C.; Jalapathy, Kripa V.; Chen, Bing; Russell, Robert G.; ***Morris, Sheldon L.*** ; Jacobs, William R. Jr [Reprint Author]
CS Howard Hughes Med Inst, Albert Einstein Coll Med, 1300 Morris Pk Ave, Bronx, NY, 10461, USA
jacobsw@hhmi.org
SO Infection and Immunity, (February 2005) Vol. 73, No. 2, pp. 1196-1203. print.
ISSN: 0019-9567 (ISSN print).
DT Article
LA English
ED Entered STN: 4 May 2005
Last Updated on STN: 4 May 2005

L12 ANSWER 5 OF 5 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN DUPLICATE 2
AN 2002:542024 BIOSIS <<LOGINID::20091103>>
DN PREV200200542024
TI A ***pantothenate*** ***auxotroph*** of Mycobacterium tuberculosis is highly attenuated and protects mice against tuberculosis.
AU Sambandamurthy, Vasan K.; Wang, Xiaojuan; Chen, Bing; Russell, Robert G.;

Derrick, Steven; Collins, Frank M.; ***Morris, Sheldon L.*** ; Jacobs, William R., Jr. [Reprint author]

CS Department of Microbiology and Immunology, Howard Hughes Medical Institute, Bronx, NY, USA
jacobsw@hhmi.org

SO Nature Medicine, (October, 2002) Vol. 8, No. 10, pp. 1171-1174. print.
ISSN: 1078-8956.
DT Article
LA English
ED Entered STN: 23 Oct 2002
Last Updated on STN: 23 Oct 2002

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L13          0 ("BARDAROV STOYAN"/AU OR "BARDAROV STOYAN S"/AU) AND AUXOTROPH
               AND PANTOTHENATE

=> s e1-e4 and auxotroph and pantothenate
L14          0 ("BARDAROV S S"/AU OR "BARDAROV SAVCO"/AU OR "BARDAROV STOYAN"/A
               U OR "BARDAROV STOYAN S"/AU) AND AUXOTROPH AND PANTOTHENATE

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=> s e1-e4 and auxotroph and pantothenate
L15          1 ("BARDAROV STOYAN"/AU OR "BARDAROV STOYAN S"/AU OR "BARDAROV
               SVETOSLAV"/AU OR "BARDAROV SVETOSLAV JR"/AU) AND AUXOTROPH AND
               PANTOTHENATE

=> d

L15  ANSWER 1 OF 1  SCISEARCH  COPYRIGHT (c) 2009 The Thomson Corporation  on
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STN
AN 2006:1074555 SCISEARCH <<LOGINID::20091103>>
GA The Genuine Article (R) Number: 099NA
TI Protection elicited by two glutamine auxotrophs of Mycobacterium tuberculosis and in vivo growth phenotypes of the four unique glutamine synthetase mutants in a murine model
AU Jacobs, William R., Jr. (Reprint)
CS Albert Einstein Coll Med, Howard Hughes Med Inst, 1300 Morris Pk Ave, Bronx, NY 10461 USA (Reprint)
AU Lee, Sunhee; Jeon, Bo-Young; ***Bardarov, Svetoslav*** ; Chen, Mei; Morris, Sheldon L.
CS Albert Einstein Coll Med, Howard Hughes Med Inst, Bronx, NY 10461 USA; Albert Einstein Coll Med, Dept Microbiol & Immunol, Bronx, NY 10461 USA; US FDA, Ctr Biol Evaluat & Res, Bethesda, MD 20014 USA; Univ Massachusetts, Dept Pathol, Worcester, MA 01605 USA
E-mail: jacobsw@hhmi.org
CYA USA
SO INFECTION AND IMMUNITY, (NOV 2006) Vol. 74, No. 11, pp. 6491-6495. ISSN: 0019-9567.
PB AMER SOC MICROBIOLOGY, 1752 N ST NW, WASHINGTON, DC 20036-2904 USA.
DT Article; Journal
LA English
REC Reference Count: 27
ED Entered STN: 16 Nov 2006
Last Updated on STN: 16 Nov 2006
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

=> s mycobacter? and auxotroph?
L17 714 MYCOBACTER? AND AUXOTROPH?

=> s l17 and (pantothenate or RD1 or panCD)
L18 64 L17 AND (PANTOTHENATE OR RD1 OR PANCD)

=> dup rem l18
PROCESSING COMPLETED FOR L18
L19 36 DUP REM L18 (28 DUPLICATES REMOVED)

=> d bib ab kwic 1-
YOU HAVE REQUESTED DATA FROM 36 ANSWERS - CONTINUE? Y/(N):y

L19 ANSWER 1 OF 36 CAPLUS COPYRIGHT 2009 ACS on STN
AN 2009:53750 CAPLUS <<LOGINID::20091103>>
DN 150:142460
TI Engineered ***Mycobacterial*** strains modulating IL-12 and its uses as vaccines for improved immune responses
IN Jacobs, William R., Jr.; Lawrence, Kari; Dao, Dee; Porcelli, Steven A.; Chan, John; Hsu, Tsungda
PA Albert Einstein College of Medicine of Yeshiva University, USA
SO PCT Int. Appl., 70pp., which
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2009008912	A2	20090115	WO 2008-US3204	20080310

W: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRAI US 2007-918997P P 20070319
US 2007-930839P P 20070517

AB Provided are ***mycobacteria*** deleted in at least a portion of a region 3 ESAT-6-like gene cluster. Also provided are ***mycobacteria*** comprising a mutation in an roc-1 gene. Addnl., vaccines comprising these ***mycobacteria*** are provided. Further provided are methods of making a recombinant ***mycobacterium*** , methods of modulating an immune response in a mammal, methods of inhibiting IL- 12 prodn. in a mammal, and methods of stimulating IL-12 prodn. in a mammal. Vaccine adjuvants are also provided, as are methods of modulating immunity to a target antigen in a mammal. Deletions of esat-6/cfp-O10 from R3 alone, as well as the entire region were generated in M smegmatis. It was confirmed that the entire R3 deletion from M tuberculosis was essential, whereas the esat-6/cfp-10 deletion is not. The R3 mutant in M smegmatis upregulated IL-12 transcription, whereas the esat-6/cfp-10 deletion had no effect on IL-12 in M smegmatis or M.tuberculosis. Further, complementation of the M. smegmatis R3 deletion with M tuberculosis R3 restored the IL-12 suppressive phenotype.

TI Engineered ***Mycobacterial*** strains modulating IL-12 and its uses as vaccines for improved immune responses

AB Provided are ***mycobacteria*** deleted in at least a portion of a region 3 ESAT-6-like gene cluster. Also provided are ***mycobacteria*** comprising a mutation in an roc-1 gene. Addnl., vaccines comprising these ***mycobacteria*** are provided. Further provided are methods of making a recombinant ***mycobacterium*** , methods of modulating an immune response in a mammal, methods of inhibiting IL- 12 prodn. in a mammal, and methods. . .

IT Esophageal disease
(Achalasia, treatment of; engineered ***Mycobacterial*** strains modulating IL-12 and its uses as vaccines for improved immune responses)

IT Pneumonitis
(Autoimmune, treatment of; engineered ***Mycobacterial*** strains modulating IL-12 and its uses as vaccines for improved immune responses)

IT Bacteremia
(Disseminated, treatment of; engineered ***Mycobacterial*** strains modulating IL-12 and its uses as vaccines for improved immune responses)

IT Gene, microbial
RL: BSU (Biological study, unclassified); REM (Removal or disposal); BIOL (Biological study); PROC (Process)
(ESAT-6-like gene cluster, deletion of; engineered

Mycobacterial strains modulating IL-12 and its uses as vaccines
for improved immune responses)
IT Epididymis
(Epididymitis, treatment of; engineered ***Mycobacterial*** strains modulating IL-12 and its uses as vaccines for improved immune responses)
IT Inflammation
(Epiglottitis, treatment of; engineered ***Mycobacterial*** strains modulating IL-12 and its uses as vaccines for improved immune responses)
IT Inflammation
(Fasciitis, treatment of; engineered ***Mycobacterial*** strains modulating IL-12 and its uses as vaccines for improved immune responses)
IT Kidney disease
(Goodpasture syndrome, treatment of; engineered ***Mycobacterial*** strains modulating IL-12 and its uses as vaccines for improved immune responses)
IT Kidney disease
(IgA nephropathy, treatment of; engineered ***Mycobacterial*** strains modulating IL-12 and its uses as vaccines for improved immune responses)
IT Immune disease
(Immune complex disease, treatment of; engineered ***Mycobacterial*** strains modulating IL-12 and its uses as vaccines for improved immune responses)
IT Bone, disease
(Paget's, treatment of; engineered ***Mycobacterial*** strains modulating IL-12 and its uses as vaccines for improved immune responses)
IT Genetic element
RL: BSU (Biological study, unclassified); REM (Removal or disposal); BIOL (Biological study); PROC (Process)
(R3, deletion of; engineered ***Mycobacterial*** strains modulating IL-12 and its uses as vaccines for improved immune responses)
IT Genetic element
RL: BSU (Biological study, unclassified); REM (Removal or disposal); BIOL (Biological study); PROC (Process)
(***RD1*** , deletion of, in attenuation of ***Mycobacterium*** ; engineered ***Mycobacterial*** strains modulating IL-12 and its uses as vaccines for improved immune responses)
IT Arthritis
(Reiter's syndrome, treatment of; engineered ***Mycobacterial*** strains modulating IL-12 and its uses as vaccines for improved immune responses)
IT Abortion
(Septic, treatment of; engineered ***Mycobacterial*** strains modulating IL-12 and its uses as vaccines for improved immune responses)
IT Immunostimulants
(adjuvants; engineered ***Mycobacterial*** strains modulating IL-12 and its uses as vaccines for improved immune responses)
IT Respiratory distress syndrome
(adult, treatment of; engineered ***Mycobacterial*** strains modulating IL-12 and its uses as vaccines for improved immune responses)

IT Transplant rejection
(allotransplant, treatment of; engineered ***Mycobacterial*** strains modulating IL-12 and its uses as vaccines for improved immune responses)
IT Inflammation
Spinal column, disease
(ankylosing spondylitis, treatment of; engineered ***Mycobacterial*** strains modulating IL-12 and its uses as vaccines for improved immune responses)
IT Antiarteriosclerotics
(antiatherosclerotics; engineered ***Mycobacterial*** strains modulating IL-12 and its uses as vaccines for improved immune responses)
IT Eubacteria
Pathogen
Virus
(antigen gene expression; engineered ***Mycobacterial*** strains modulating IL-12 and its uses as vaccines for improved immune responses)
IT Macrophage
(apoptosis of, induction by ***Mycobacterium*** ; engineered ***Mycobacterial*** strains modulating IL-12 and its uses as vaccines
for improved immune responses)
IT Autoimmune disease
Inflammation
Thyroid gland, disease
(autoimmune thyroiditis, treatment of; engineered ***Mycobacterial*** strains modulating IL-12 and its uses as vaccines for improved immune responses)
IT Amino acids
Vitamins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(***auxotrophy*** for, in attenuation of ***Mycobacterium*** ; engineered ***Mycobacterial*** strains modulating IL-12 and its uses as vaccines for improved immune responses)
IT Urethra
(disease, urethritis, treatment of; engineered ***Mycobacterial*** strains modulating IL-12 and its uses as vaccines for improved immune responses)
IT Allergy inhibitors
Anti-AIDS agents
Anti-Alzheimer's agents
Anti-inflammatory agents
Anti-ischemic agents
Antiarthritics
Antiasthmatics
Antibacterial agents
Antidiabetic agents
Antifibrotic agents
Antimalarials
Antirheumatic agents
Antitumor agents
Antiulcer agents
Antiviral agents
Complementation (genetic)
Genetic engineering

Human
Immunization
Mycobacterium
Mycobacterium avium
Mycobacterium avium paratuberculosis
Mycobacterium bovis
Mycobacterium fortuitum
Mycobacterium habana
Mycobacterium intracellulare
Mycobacterium kansasii
Mycobacterium lufu
Mycobacterium phlei
Mycobacterium scrofulaceum
Mycobacterium smegmatis
Mycobacterium tuberculosis
Vaccines
Virulence (microbial)
(engineered ***Mycobacterial*** strains modulating IL-12 and its uses as vaccines for improved immune responses)

IT Interleukin 12
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(engineered ***Mycobacterial*** strains modulating IL-12 and its uses as vaccines for improved immune responses)

IT Antigens
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(engineered ***Mycobacterial*** strains modulating IL-12 and its uses as vaccines for improved immune responses)

IT Granuloma
(eosinophilic, treatment of; engineered ***Mycobacterial*** strains modulating IL-12 and its uses as vaccines for improved immune responses)

IT Parasite
(eukaryote, antigen gene expression; engineered ***Mycobacterial*** strains modulating IL-12 and its uses as vaccines for improved immune responses)

IT Promoter (genetic element)
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(for antigen gene expression; engineered ***Mycobacterial*** strains modulating IL-12 and its uses as vaccines for improved immune responses)

IT Transplant and Transplantation
(graft-vs.-host reaction, treatment of; engineered ***Mycobacterial*** strains modulating IL-12 and its uses as vaccines for improved immune responses)

IT Lung disease
(granulomatous, treatment of; engineered ***Mycobacterial*** strains modulating IL-12 and its uses as vaccines for improved immune responses)

IT Cyst, pathological
(hydatid, treatment of; engineered ***Mycobacterial*** strains modulating IL-12 and its uses as vaccines for improved immune responses)

IT Tumor necrosis factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)

(induction of; engineered ***Mycobacterial*** strains modulating IL-12 and its uses as vaccines for improved immune responses)
IT Respiratory syncytial virus
(infection, treatment of; engineered ***Mycobacterial*** strains modulating IL-12 and its uses as vaccines for improved immune responses)
IT Reperfusion
Spinal cord disease
(injury, treatment of; engineered ***Mycobacterial*** strains modulating IL-12 and its uses as vaccines for improved immune responses)
IT Diabetes mellitus
(insulin-dependent, treatment of; engineered ***Mycobacterial*** strains modulating IL-12 and its uses as vaccines for improved immune responses)
IT Animal cell
(mammalian; engineered ***Mycobacterial*** strains modulating IL-12 and its uses as vaccines for improved immune responses)
IT Nerve, disease
Pain
(neuralgia, treatment of; engineered ***Mycobacterial*** strains modulating IL-12 and its uses as vaccines for improved immune responses)
IT Inflammation
Nerve, disease
(neuritis, treatment of; engineered ***Mycobacterial*** strains modulating IL-12 and its uses as vaccines for improved immune responses)
IT Gene, microbial
RL: BSU (Biological study, unclassified); REM (Removal or disposal); BIOL (Biological study); PROC (Process)
(nlaA, deletion of, in attenuation of ***Mycobacterium*** ; engineered ***Mycobacterial*** strains modulating IL-12 and its uses as vaccines for improved immune responses)
IT Gene, microbial
RL: BSU (Biological study, unclassified); REM (Removal or disposal); BIOL (Biological study); PROC (Process)
(nuoG, deletion of, in attenuation of ***Mycobacterium*** ; engineered ***Mycobacterial*** strains modulating IL-12 and its uses as vaccines for improved immune responses)
IT Apoptosis
(of macrophage, induction by ***Mycobacterium*** ; engineered ***Mycobacterial*** strains modulating IL-12 and its uses as vaccines
for improved immune responses)
IT Eye, disease
Inflammation
(ophthalmitis, Autoimmune, treatment of; engineered ***Mycobacterial*** strains modulating IL-12 and its uses as vaccines
for improved immune responses)
IT Inflammation
Pericardium
(pericarditis, treatment of; engineered ***Mycobacterial*** strains modulating IL-12 and its uses as vaccines for improved immune responses)
IT Arteritis

Inflammation
(polyarteritis nodosa, treatment of; engineered ***Mycobacterial*** strains modulating IL-12 and its uses as vaccines for improved immune responses)

IT Enterocolitis
(pseudomembranous, treatment of; engineered ***Mycobacterial*** strains modulating IL-12 and its uses as vaccines for improved immune responses)

IT Granulomatous disease
(pulmonary, treatment of; engineered ***Mycobacterial*** strains modulating IL-12 and its uses as vaccines for improved immune responses)

IT Injury
(reperfusion, treatment of; engineered ***Mycobacterial*** strains modulating IL-12 and its uses as vaccines for improved immune responses)

IT Gene, microbial
RL: BSU (Biological study, unclassified); REM (Removal or disposal); BIOL (Biological study); PROC (Process)
(roc-1, deletion of, in attenuation of ***Mycobacterium*** ; engineered ***Mycobacterial*** strains modulating IL-12 and its uses as vaccines for improved immune responses)

IT Gene, microbial
RL: BSU (Biological study, unclassified); REM (Removal or disposal); BIOL (Biological study); PROC (Process)
(secA2, deletion of, in attenuation of ***Mycobacterium*** ; engineered ***Mycobacterial*** strains modulating IL-12 and its uses as vaccines for improved immune responses)

IT Shock (circulatory collapse)
(septic, treatment of; engineered ***Mycobacterial*** strains modulating IL-12 and its uses as vaccines for improved immune responses)

IT Inflammation
Vein, disease
(thrombophlebitis, treatment of; engineered ***Mycobacterial*** strains modulating IL-12 and its uses as vaccines for improved immune responses)

IT Inflammation
Thyroid gland, disease
(thyroiditis, treatment of; engineered ***Mycobacterial*** strains modulating IL-12 and its uses as vaccines for improved immune responses)

IT AIDS (disease)
Allergy
Alveolitis
Alzheimer disease
Amebiasis
Anaphylaxis
Appendicitis
Arteritis
Arthralgia
Arthritis
Asthma
Atherosclerosis
Autoimmune disease
Behcet's syndrome
Brain infarction

Bronchiolitis
Bronchitis
Burn
Cachexia
Candidiasis
Celiac disease
Cholangitis
Cholecystitis
Colitis
Crohn disease
Cystic fibrosis
Dengue fever
Dermatitis
Dermatomyositis
Diverticulitis
Duodenal ulcer
Emphysema
Encephalitis
Endocarditis
Enteritis
Fever and Hyperthermia
Filariasis
Gastric ulcer
Gout
Guillain-Barre syndrome
Hay fever
Heart failure
Hemorrhagic colitis
Hepatitis
Hepatitis B
Hepatitis C
Herpes
Hodgkin's disease
Ileus
Influenza
Ischemia
Malaria
Meningitis
Multiple sclerosis
Myasthenia gravis
Myocardial ischemia
Myocarditis
Necrosis
Neoplasm
Osteomyelitis
Pancreatitis
Paralysis
Peptic ulcer
Periodontal disease
Peritonitis
Pharyngitis
Pleurisy
Prostatitis
Rheumatic fever
Rheumatoid arthritis
Rhinitis
Sarcoidosis

Sepsis
Septicemia
Sinusitis
Stroke
Sunburn
Synovitis
Systemic lupus erythematosis
Ulcerative colitis
Urticaria
Uveitis
Vasculitis
Wart
Whipple disease
(treatment of; engineered ***Mycobacterial*** strains modulating IL-12 and its uses as vaccines for improved immune responses)

IT Mycolic acids
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(trehalose esters; engineered ***Mycobacterial*** strains modulating IL-12 and its uses as vaccines for improved immune responses)

IT Vaccines
(tumor; engineered ***Mycobacterial*** strains modulating IL-12 and its uses as vaccines for improved immune responses)

IT Inflammation
(urethritis, treatment of; engineered ***Mycobacterial*** strains modulating IL-12 and its uses as vaccines for improved immune responses)

IT Antitumor agents
(vaccines; engineered ***Mycobacterial*** strains modulating IL-12 and its uses as vaccines for improved immune responses)

IT Inflammation
Vaginal disease
(vaginitis, treatment of; engineered ***Mycobacterial*** strains modulating IL-12 and its uses as vaccines for improved immune responses)

IT Skin, disease
(wheal-flare reaction, treatment of; engineered ***Mycobacterial*** strains modulating IL-12 and its uses as vaccines for improved immune responses)

IT Interferons
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(.gamma., induction of; engineered ***Mycobacterial*** strains modulating IL-12 and its uses as vaccines for improved immune responses)

IT 99-20-7D, Trehalose, dimycolate
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(engineered ***Mycobacterial*** strains modulating IL-12 and its uses as vaccines for improved immune responses)

IT 1100373-84-9 1100373-86-1 1100373-88-3 1100373-89-4 1100373-90-7
1100373-91-8 1100373-92-9 1100373-93-0 1100373-94-1 1100373-96-3
1100373-97-4
RL: PRP (Properties)
(unclaimed nucleotide sequence; engineered ***Mycobacterial*** strains modulating IL-12 and its uses as vaccines for improved immune responses)

IT 1100373-85-0
RL: PRP (Properties)
(unclaimed protein sequence; engineered ***Mycobacterial*** strains modulating IL-12 and its uses as vaccines for improved immune responses)

L19 ANSWER 2 OF 36 MEDLINE on STN
AN 2009419014 IN-PROCESS <<LOGINID::20091103>>
DN PubMed ID: 19526063
TI Delineating bacteriostatic and bactericidal targets in ***mycobacteria*** using IPTG inducible antisense expression.
AU Kaur Parvinder; Agarwal Saurabh; Datta Santanu
CS AstraZeneca India Pvt Ltd, Hebbal, Bangalore, India.
SO PloS one, (2009) Vol. 4, No. 6, pp. e5923. Electronic Publication: 2009-06-15.
Journal code: 101285081. E-ISSN: 1932-6203.
Report No.: NLM-PMC2691988.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LA English
FS NONMEDLINE; IN-PROCESS; NONINDEXED; Priority Journals
ED Entered STN: 16 Jun 2009
Last Updated on STN: 19 Jun 2009
AB In order to identify novel high value antibacterial targets it is desirable to delineate whether the inactivation of the target enzyme will lead to bacterial death or stasis. This knowledge is particularly important in slow growing organisms, like ***mycobacteria*** , where most of the viable anti-tubercular agents are bactericidal. A bactericidal target can be identified through the conditional deletion or inactivation of the target gene at a relatively high cell number and subsequently following the time course of survival for the bacteria. A simple protocol to execute conditional inactivation of a gene is by antisense expression. We have developed a ***mycobacteria*** specific IPTG inducible vector system and monitored the effect of antisense inhibition of several known essential genes in ***mycobacteria*** by following their survival kinetics. By this method, we could differentiate between genes whose down regulation lead to bacteriostatic or bactericidal effect. Targets for standard anti-tubercular drugs like inhA for isoniazid, rpoB and C for rifampicin, and gyr A/B for flouroquinolones were shown to be bactericidal. In contrast targets like FtsZ behaved in a bacteriostatic manner. Induction of antisense expression in embB and ribosomal RNA genes, viz., rplJ and rpsL showed only a marginal growth inhibition. The specificity of the antisense inhibition was conclusively shown in the case of ***auxotrophic*** gene ilvB. The bactericidal activity following antisense expression of ilvB was completely reversed when the growth media was supplemented with the isoleucine, leucine, valine and ***pantothenate*** . Additionally, under these conditions the expression of several genes in branched chain amino acid pathway was severely suppressed indicating targeted gene inactivation.
TI Delineating bacteriostatic and bactericidal targets in ***mycobacteria*** using IPTG inducible antisense expression.
AB . . . the target enzyme will lead to bacterial death or stasis. This knowledge is particularly important in slow growing organisms, like ***mycobacteria*** , where most of the viable anti-tubercular agents are bactericidal. A bactericidal target can be identified through the conditional deletion or. . . the bacteria. A simple protocol to

execute conditional inactivation of a gene is by antisense expression. We have developed a ***mycobacteria*** specific IPTG inducible vector system and monitored the effect of antisense inhibition of several known essential genes in ***mycobacteria*** by following their survival kinetics. By this method, we could differentiate between genes whose down regulation lead to bacteriostatic or. . . rpsL showed only a marginal growth inhibition. The specificity of the antisense inhibition was conclusively shown in the case of ***auxotrophic*** gene ilvB. The bactericidal activity following antisense expression of ilvB was completely reversed when the growth media was supplemented with the isoleucine, leucine, valine and ***pantothenate*** . Additionally, under these conditions the expression of several genes in branched chain amino acid pathway was severely suppressed indicating targeted. . .

L19 ANSWER 3 OF 36 SCISEARCH COPYRIGHT (c) 2009 The Thomson Corporation on STN
AN 2009:930391 SCISEARCH <<LOGINID::20091103>>
GA The Genuine Article (R) Number: 475IG
TI Efficacy and safety of live attenuated persistent and rapidly cleared ***Mycobacterium*** tuberculosis vaccine candidates in non-human primates
AU Larsen, Michelle H. (Reprint)
CS Albert Einstein Coll Med, 1301 Morris Pk Ave, Bronx, NY 10467 USA (Reprint)
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CS AstraZeneca, Bangalore, Karnataka, India
AU Lackner, Andrew A.; Aye, Pyone Pyone; Didier, Peter
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AU Huang, Dan; Shao, Linyun; Wei, Huiyong; Chen, Zheng W.
CS Univ Illinois, Coll Med, Chicago, IL USA
AU Huang, Dan; Shao, Linyun; Wei, Huiyong; Chen, Zheng W.
CS Ctr Primate Biomed Res, Dept Microbiol & Immunol, Chicago, IL 60612 USA
AU Letvin, Norman L.
CS Harvard Univ, Beth Israel Deaconess Med Ctr, Sch Med, Boston, MA 02215 USA
AU Frothingham, Richard; Haynes, Barton F.
CS Duke Univ, Duke Human Vaccine Inst, Durham, NC 27710 USA
CYA USA; India
SO VACCINE, (23 JUL 2009) Vol. 27, No. 34, pp. 4709-4717.
ISSN: 0264-410X.
PB ELSEVIER SCI LTD, THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD OX5 1GB, OXON, ENGLAND.
DT Article; Journal
LA English
REC Reference Count: 29
ED Entered STN: 6 Aug 2009
Last Updated on STN: 6 Aug 2009
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Tuberculosis (TB) remains a global health burden for which safe vaccines are needed. BCG has limitations as a TB vaccine so we have focused on live attenuated ***Mycobacterium*** tuberculosis mutants as vaccine candidates. Prior to human studies, however, it is necessary to demonstrate safety in non-human primates (NHP). In this study, we

evaluate the safety and efficacy of two live attenuated M. tuberculosis double deletion vaccine strains mc(2)6020 (Delta lysA Delta ***panCD***) and mc(2)6030 (Delta ***RD1*** Delta ***panCD***) in cynomolgus macaques. In murine models, mc(2)6020 is rapidly cleared while mc(2)6030 persists. Both mc(2)6020 and mc(2)6030 were safe and well tolerated in cynomolgus macaques. Following a high-dose intrabronchial challenge with virulent M. tuberculosis, mc(2)6020-vaccinates were afforded a level of protection intermediate between that elicited by BCG vaccination and no vaccination. BCG vaccinates had reduced tuberculosis-associated pathology and improved clinical scores as compared to saline and mc(2)6030 vaccinates, but survival did not differ among the groups. (C) 2009 Elsevier Ltd. All rights reserved.

TI Efficacy and safety of live attenuated persistent and rapidly cleared ***Mycobacterium*** tuberculosis vaccine candidates in non-human primates

AB . . . for which safe vaccines are needed. BCG has limitations as a TB vaccine so we have focused on live attenuated ***Mycobacterium*** tuberculosis mutants as vaccine candidates. Prior to human studies, however, it is necessary to demonstrate safety in non-human primates (NHP).. . . we evaluate the safety and efficacy of two live attenuated M. tuberculosis double deletion vaccine strains mc(2)6020 (Delta lysA Delta ***panCD***) and mc(2)6030 (Delta ***RD1*** Delta ***panCD***) in cynomolgus macaques. In murine models, mc(2)6020 is rapidly cleared while mc(2)6030 persists. Both mc(2)6020 and mc(2)6030 were safe and. . .

ST Author Keywords: Vaccine; ***Mycobacteria*** ; ***Mycobacterium*** ; Tuberculosis; Non-human primate; BCG; Safety

STP KeyWords Plus (R): BACILLE-CALMETTE-GUERIN; DELTA- ***RD1*** DELTA- ***PANCD*** ; T-CELL RESPONSES; ***PANTOTHENATE*** ***AUXOTROPH*** ; CYNOMOLGUS MONKEY; BCG VACCINATION; INFECTION; PROTECTION; MACAQUES; MODEL

L19 ANSWER 4 OF 36 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN DUPLICATE 1

AN 2009:425532 BIOSIS <<LOGINID::20091103>>

DN PREV200900426635

TI Delineating Bacteriostatic and Bactericidal Targets in ***Mycobacteria*** Using IPTG Inducible Antisense Expression.

AU Kaur, Parvinder [Reprint Author]; Agarwal, Saurabh; Datta, Santanu

CS AstraZeneca India Pvt Ltd, Bangalore, Karnataka, India
santanu.datta@astrazeneca.com

SO PLoS One, (JUN 15 2009) Vol. 4, No. 6, pp. Article No.: e5923.
ISSN: 1932-6203.

DT Article

LA English

ED Entered STN: 15 Jul 2009
Last Updated on STN: 15 Jul 2009

AB In order to identify novel high value antibacterial targets it is desirable to delineate whether the inactivation of the target enzyme will lead to bacterial death or stasis. This knowledge is particularly important in slow growing organisms, like ***mycobacteria*** , where most of the viable anti-tubercular agents are bactericidal. A bactericidal target can be identified through the conditional deletion or inactivation of the target gene at a relatively high cell number and subsequently following the time course of survival for the bacteria. A simple protocol to execute conditional inactivation of a gene is by antisense expression. We have developed a ***mycobacteria*** specific

IPTG inducible vector system and monitored the effect of antisense inhibition of several known essential genes in ***mycobacteria*** by following their survival kinetics. By this method, we could differentiate between genes whose down regulation lead to bacteriostatic or bactericidal effect. Targets for standard anti-tubercular drugs like inhA for isoniazid, rpoB and C for rifampicin, and gyr A/B for flouroquinolones were shown to be bactericidal. In contrast targets like FtsZ behaved in a bacteriostatic manner. Induction of antisense expression in embB and ribosomal RNA genes, viz., rp/J and rpsL showed only a marginal growth inhibition. The specificity of the antisense inhibition was conclusively shown in the case of ***auxotrophic*** gene i/vB. The bactericidal activity following antisense expression of i/vB was completely reversed when the growth media was supplemented with the isoleucine, leucine, valine and ***pantothenate*** . Additionally, under these conditions the expression of several genes in branched chain amino acid pathway was severely suppressed indicating targeted gene inactivation.

TI Delineating Bacteriostatic and Bactericidal Targets in ***Mycobacteria*** Using IPTG Inducible Antisense Expression.

AB. . . the target enzyme will lead to bacterial death or stasis. This knowledge is particularly important in slow growing organisms, like ***mycobacteria*** , where most of the viable anti-tubercular agents are bactericidal. A bactericidal target can be identified through the conditional deletion or. . . the bacteria. A simple protocol to execute conditional inactivation of a gene is by antisense expression. We have developed a ***mycobacteria*** specific IPTG inducible vector system and monitored the effect of antisense inhibition of several known essential genes in ***mycobacteria*** by following their survival kinetics. By this method, we could differentiate between genes whose down regulation lead to bacteriostatic or. . . rpsL showed only a marginal growth inhibition. The specificity of the antisense inhibition was conclusively shown in the case of ***auxotrophic*** gene i/vB. The bactericidal activity following antisense expression of i/vB was completely reversed when the growth media was supplemented with the isoleucine, leucine, valine and ***pantothenate*** . Additionally, under these conditions the expression of several genes in branched chain amino acid pathway was severely suppressed indicating targeted. . .

IT . . .
(Biochemistry and Molecular Biophysics)

IT Chemicals & Biochemicals
leucine; isoleucine; valine; isoniazid: antibacterial-drug, antiinfective-drug; rifampicin: antibacterial-drug, antiinfective-drug; flouroquinolones: antibacterial-drug, antiinfective-drug; ***pantothenate*** ; isopropyl-beta-D-thiogalactopyranoside [IPTG]: expression

ORGN Classifier
Mycobacteriaceae 08881
Super Taxa
Mycobacteria ; Actinomycetes and Related Organisms; Eubacteria; Bacteria; Microorganisms
Organism Name
mycobacteria (common)
Taxa Notes
Bacteria, Eubacteria, Microorganisms

RN 328-39-2 (leucine)
443-79-8 (isoleucine)
516-06-3 (valine)
54-85-3 (isoniazid)

13292-46-1 (rifampicin)
20938-62-9 (***pantothenate***)
367-93-1 (isopropyl-beta-D-thiogalactopyranoside)
367-93-1 (IPTG)
GEN ***mycobacteria*** rpoB gene (***Mycobacteriaceae***);
mycobacteria embB gene (***Mycobacteriaceae***);
mycobacteria rplJ gene (***Mycobacteriaceae***): ribosomal
RNA
gene; ***mycobacteria*** rpsL gene (***Mycobacteriaceae***):
ribosomal RNA gene; ***mycobacteria*** ilvB gene (
Mycobacteriaceae): expression; ***mycobacteria*** inhA gene (
Mycobacteriaceae); ***mycobacteria*** rpoC gene (
Mycobacteriaceae); ***mycobacteria*** gyr A/B gene (
Mycobacteriaceae); ***mycobacteria*** FtsZ gene (
Mycobacteriaceae)

L19 ANSWER 5 OF 36 SCISEARCH COPYRIGHT (c) 2009 The Thomson Corporation on STN
AN 2008:1284984 SCISEARCH <<LOGINID::20091103>>
GA The Genuine Article (R) Number: 361YW
TI A Replication-Limited Recombinant ***Mycobacterium*** bovis BCG Vaccine against Tuberculosis Designed for Human Immunodeficiency Virus-Positive Persons Is Safer and More Efficacious than BCG
AU Horwitz, Marcus A. (Reprint)
CS Univ Calif Los Angeles, Sch Med, Div Infect Dis, Dept Med, CHS 37-121, 10833 Le Conte Ave, Los Angeles, CA 90095 USA (Reprint)
E-mail: MHorwitz@mednet.ucla.edu
AU Tullius, Michael V.; Harth, Guenter; Maslesa-Galic, Sasa; Dillon, Barbara J.; Horwitz, Marcus A. (Reprint)
CS Univ Calif Los Angeles, Sch Med, Div Infect Dis, Dept Med, Los Angeles, CA 90095 USA
E-mail: MHorwitz@mednet.ucla.edu
CYA USA
SO INFECTION AND IMMUNITY, (NOV 2008) Vol. 76, No. 11, pp. 5200-5214.
ISSN: 0019-9567.
PB AMER SOC MICROBIOLOGY, 1752 N ST NW, WASHINGTON, DC 20036-2904 USA.
DT Article; Journal
LA English
REC Reference Count: 53
ED Entered STN: 14 Nov 2008
Last Updated on STN: 14 Nov 2008
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Tuberculosis is the leading cause of death in AIDS patients, yet the current tuberculosis vaccine, ***Mycobacterium*** bovis bacillus Calmette-Guerin (BCG), is contraindicated for immunocompromised individuals, including human immunodeficiency virus-positive persons, because it can cause disseminated disease; moreover, its efficacy is suboptimal. To address these problems, we have engineered BCG mutants that grow normally in vitro in the presence of a supplement, are preloadable with supplement to allow limited growth in vivo, and express the highly immunoprotective ***Mycobacterium*** tuberculosis 30-kDa major secretory protein. The limited replication in vivo renders these vaccines safer than BCG in SCID mice yet is sufficient to induce potent cell-mediated and protective immunity in the outbred guinea pig model of pulmonary tuberculosis. In the case of one vaccine, rBCG(mbtB) 30, protection was superior to that with BCG (0.3-log fewer CFU of M. tuberculosis in the lung [P < 0.04] and 0.6-log fewer CFU in the spleen [P

= 0.001] in aerosol-challenged animals [means for three experiments]); hence, rBCG(mbtB) 30 is the first live ***mycobacterial*** vaccine that is both more attenuated than BCG in the SCID mouse and more potent than BCG in the guinea pig. Our study demonstrates the feasibility of developing safer and more potent vaccines against tuberculosis. The novel approach of engineering a replication-limited vaccine expressing a recombinant immunoprotective antigen and preloading it with a required nutrient, such as iron, that is capable of being stored should be generally applicable to other live vaccine vectors targeting intracellular pathogens.

TI A Replication-Limited Recombinant ***Mycobacterium*** bovis BCG Vaccine against Tuberculosis Designed for Human Immunodeficiency Virus-Positive Persons Is Safer and More Efficacious than BCG

AB Tuberculosis is the leading cause of death in AIDS patients, yet the current tuberculosis vaccine, ***Mycobacterium*** bovis bacillus Calmette-Guerin (BCG), is contraindicated for immunocompromised individuals, including human immunodeficiency virus-positive persons, because it can cause disseminated disease;. . . the presence of a supplement, are preloadable with supplement to allow limited growth in vivo, and express the highly immunoprotective ***Mycobacterium*** tuberculosis 30-kDa major secretory protein. The limited replication in vivo renders these vaccines safer than BCG in SCID mice yet. . . in the spleen [P = 0.001] in aerosol-challenged animals [means for three experiments]); hence, rBCG(mbtB) 30 is the first live ***mycobacterial*** vaccine that is both more attenuated than BCG in the SCID mouse and more potent than BCG in the guinea. . .

STP KeyWords Plus (R): GREATER PROTECTIVE IMMUNITY; MAJOR SECRETORY PROTEIN; ***PANTOTHENATE*** ***AUXOTROPH*** ; GLUTAMINE-SYNTHETASE; GUINEA-PIGS; EXTRACELLULAR PROTEINS; MUTANT STRAIN; TB VACCINE; MODEL; RESISTANCE

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AN 2009:27989 BIOSIS <<LOGINID::20091103>>

DN PREV200900027989

TI Inhibition of ***Mycobacterium*** tuberculosis ***Pantothenate*** Synthetase by Analogues of the Reaction Intermediate.

AU Ciulli, Alessio [Reprint Author]; Scott, Duncan E.; Ando, Michiyo; Reyes, Fernando; Saldanha, S. Adrian; Tuck, Kellie L.; Chirgadze, Dimitri Y.; Blundell, Tom L.; Abell, Chris

CS Univ Cambridge, Univ Chem Lab, Lensfield Rd, Cambridge CB2 1EW, UK
ac313@cam.ac.uk; ca26@cam.ac.uk

SO ChemBioChem, (NOV 3 2008) Vol. 9, No. 16, pp. 2606-2611.
ISSN: 1439-4227.

DT Article

LA English

ED Entered STN: 24 Dec 2008
Last Updated on STN: 24 Dec 2008

TI Inhibition of ***Mycobacterium*** tuberculosis ***Pantothenate*** Synthetase by Analogues of the Reaction Intermediate.

IT . . .
control, symptom, diagnosis, etiology
Tuberculosis (MeSH)

IT Chemicals & Biochemicals
ATP; magnesium(II) ion; beta-alanine; pyrophosphate; AMP; inhibitors; water molecule; antimicrobial agents; ***pantothenate*** synthetase [EC 6.3.2.1]; genome; pantoate; human vaccine candidate;

pantothenate : biosynthesis; ***pantothenate*** permase; panF homologue; M. tuberculosis genome; salicyl adenylate intermediate; sulfamoyl adenylate mimic

ORGN . . .

Taxa

Primates; Mammalia; Vertebrata; Chordata; Animalia

Organism Name

human (common)

Taxa Notes

Animals, Chordates, Humans, Mammals, Primates, Vertebrates

ORGN Classifier

Mycobacteriaceae 08881

Super Taxa

Mycobacteria ; Actinomycetes and Related Organisms; Eubacteria; Bacteria; Microorganisms

Organism Name

Mycobacterium tuberculosis (species): ***pantothenate*** ***auxotroph*** , multiple-drug-resistant strain, strain-bacille Calmette-Guerin

Taxa Notes

Bacteria, Eubacteria, Microorganisms

RN 111839-44-2 (ATP)
22537-22-0 (magnesium(II) ion)
107-95-9 (beta-alanine)
14000-31-8 (pyrophosphate)
177933-73-2 (AMP)
20938-62-9 (***pantothenate***)

GEN human panB gene (Hominidae); human panE gene (Hominidae); human panD gene (Hominidae); human panC gene (Hominidae); human ***panCD*** gene (Hominidae); human panF gene (Hominidae)

L19 ANSWER 7 OF 36 SCISEARCH COPYRIGHT (c) 2009 The Thomson Corporation on STN

AN 2008:489650 SCISEARCH <<LOGINID::20091103>>

GA The Genuine Article (R) Number: 284LY

TI 5-tert-butyl-N-pyrazol-4-yl-4,5,6,7-tetrahydrobenzo[d]isoxazole-3-carboxamide derivatives as novel potent inhibitors of ***Mycobacterium*** tuberculosis ***pantothenate*** synthetase: Initiating a quest for new antitubercular drugs

AU Petukhov, Pavel A. (Reprint)
CS Univ Illinois, Coll Pharm, Dept Med Chem & Pharmacognosy, 833 S Wood St, Chicago, IL 60612 USA (Reprint)
AU Velaparthi, Subash; Brunsteiner, Michael; Uddin, Reaz; Wan, Baojie; Franzblau, Scott G.
CS Univ Illinois, Coll Pharm, Dept Med Chem & Pharmacognosy, Chicago, IL 60612 USA; Univ Illinois, Coll Pharm, Inst TB Res, Chicago, IL 60612 USA
E-mail: pap4@uic.edu
CYA USA

SO JOURNAL OF MEDICINAL CHEMISTRY, (10 APR 2008) Vol. 51, No. 7, pp. 1999-2002.
ISSN: 0022-2623.
PB AMER CHEMICAL SOC, 1155 16TH ST, NW, WASHINGTON, DC 20036 USA.
DT Article; Journal
LA English
REC Reference Count: 27
ED Entered STN: 17 Apr 2008
Last Updated on STN: 3 Jul 2008

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB ***Pantothenate*** synthetase (PS) is one of the potential new antimicrobial targets that may also be useful for the treatment of the nonreplicating persistent forms of ***Mycobacterium*** tuberculosis. In this Letter we present a series of 5-tert-butyl-N-pyrazol-4-yl-4,5,6,7-tetrahydrobenzo[d]isoxazole-3-carboxamide derivatives as novel potent ***Mycobacterium*** tuberculosis PS inhibitors, their in silico molecular design, synthesis, and inhibitory activity.

TI 5-tert-butyl-N-pyrazol-4-yl-4,5,6,7-tetrahydrobenzo[d]isoxazole-3-carboxamide derivatives as novel potent inhibitors of ***Mycobacterium*** tuberculosis ***pantothenate*** synthetase: Initiating a quest for new antitubercular drugs

AB ***Pantothenate*** synthetase (PS) is one of the potential new antimicrobial targets that may also be useful for the treatment of the nonreplicating persistent forms of ***Mycobacterium*** tuberculosis. In this Letter we present a series of 5-tert-butyl-N-pyrazol-4-yl-4,5,6,7-tetrahydrobenzo[d]isoxazole-3-carboxamide derivatives as novel potent ***Mycobacterium*** tuberculosis PS inhibitors, their in silico molecular design, synthesis, and inhibitory activity.

STP KeyWords Plus (R): GENE-EXPRESSION; INFECTION; ***AUXOTROPH*** ; DESIGN; STATE; ASSAY

L19 ANSWER 8 OF 36 SCISEARCH COPYRIGHT (c) 2009 The Thomson Corporation on STN

AN 2008:1203532 SCISEARCH <<LOGINID::20091103>>

GA The Genuine Article (R) Number: 353UE

TI Construction of a severely attenuated mutant of ***Mycobacterium*** tuberculosis for reducing risk to laboratory workers

AU Movahedzadeh, Farahnaz (Reprint)

CS Univ Illinois, Inst TB Res, Coll Pharm, Room 412, Chicago, IL 60612 USA (Reprint)

AU Williams, Ann; Clark, Simon; Hatch, Graham; Smith, Debbie; ten Bokum, Annemieke; Parish, Tanya; Bacon, Joanna; Stoker, Neil

CS Univ London Royal Vet Coll, Dept Pathol & Infect Dis, London NW1 0TU, England; Hlth Protect Agcy Ctr Emergency Preparedness & Re, Salisbury SP4 0JG, Wilts, England; London Sch Hyg & Trop Med, Dept Infect & Trop Dis, London WC1E 7HT, England; Ctr Infect Dis, London E1 2AT, England

E-mail: movahed@uic.edu

CYA USA; England

SO TUBERCULOSIS, (SEP 2008) Vol. 88, No. 5, pp. 375-381.
ISSN: 1472-9792.

PB CHURCHILL LIVINGSTONE, JOURNAL PRODUCTION DEPT, ROBERT STEVENSON HOUSE, 1-3 BAXTERS PLACE, LEITH WALK, EDINBURGH EH1 3AF, MIDLOTHIAN, SCOTLAND.

DT Article; Journal

LA English

REC Reference Count: 28

ED Entered STN: 16 Oct 2008
Last Updated on STN: 16 Oct 2008

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The ability to construct defined deletions of ***Mycobacterium*** tuberculosis has allowed many genes involved in virulence to be identified. Deletion of nutritional genes leads to varying levels of attenuation, presumably reflecting the need for a particular molecule, and the availability (or tack) of that molecule in vivo. We have previously shown that M. tuberculosis mutants lacking either the trpD or ino1 gene

are highly attenuated in mouse models of infection, but can grow when supplemented with tryptophan or inositol, respectively. In this paper we have constructed a double Delta trpD Delta ino1 mutant, and show that this is severely attenuated in SCID mouse and guinea pig models. As the strain will grow in the presence of supplements, we propose that this strain could be used for research and antigen preparative purposes, with reduced risks to laboratory workers. (c) 2008 Elsevier Ltd. All rights reserved.

TI Construction of a severely attenuated mutant of ***Mycobacterium*** tuberculosis for reducing risk to laboratory workers

AB The ability to construct defined deletions of ***Mycobacterium*** tuberculosis has allowed many genes involved in virulence to be identified. Deletion of nutritional genes leads to varying levels of. . .

STP KeyWords Plus (R): GUINEA-PIGS; ***PANTOTHENATE*** ***AUXOTROPH*** ; PROTECTIVE IMMUNITY; ENHANCED PROTECTION; GRANULOMA-FORMATION; CALMETTE-GUERIN; BCG; BOVIS; VACCINATION; VACCINES

L19 ANSWER 9 OF 36 SCISEARCH COPYRIGHT (c) 2009 The Thomson Corporation on STN

AN 2008:258059 SCISEARCH <<LOGINID::20091103>>

GA The Genuine Article (R) Number: 258OX

TI Live tuberculosis vaccines based on phoP mutants: a step towards clinical trials

AU Martin, Carlos (Reprint)

CS Univ Zaragoza, Grp Genet Micobacterias, CIBER Enfermedades Resp, Dept Microbiol, Fac Med, C-Domingo Miral SN, E-50009 Zaragoza, Spain (Reprint)

AU Asensio, Jesus A. Gonzalo; Arbues, Ainhoa; Perez, Esther; Gicquel, Brigitte

CS Univ Zaragoza, Grp Genet Micobacterias, CIBER Enfermedades Resp, Dept Microbiol, Fac Med, E-50009 Zaragoza, Spain; GlaxoSmithKline Inc, GSK 1 D DDW, Parque Tecnol Madrid, Madrid 28760, Spain; Inst Pasteur, Unite Genet Mycobacterienne, Paris, France

E-mail: carlos@unizar.es

CYA Spain; France

SO EXPERT OPINION ON BIOLOGICAL THERAPY, (FEB 2008) Vol. 8, No. 2, pp. 201-211.

ISSN: 1471-2598.

PB INFORMA HEALTHCARE, TELEPHONE HOUSE, 69-77 PAUL STREET, LONDON EC2A 4LQ, ENGLAND.

DT General Review; Journal

LA English

REC Reference Count: 86

ED Entered STN: 28 Feb 2008

Last Updated on STN: 28 Feb 2008

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Bacillus Calmette-Guerin (BCG) is the only preventive treatment for tuberculosis in humans, but this live vaccine confers variable protection against pulmonary tuberculosis in adults. Advances in the understanding of ***Mycobacterium*** tuberculosis immunopathogenesis have renewed hopes of developing new prophylactic vaccines conferring better protection than BCG. The authors describe here state-of-the-art attenuated live vaccines based on inactivation of the phoP gene, a transcriptional regulator of key virulence networks in M. tuberculosis. Recent preclinical testing of live vaccines based on phoP inactivation has demonstrated proof of concept, with a high degree of attenuation and protection against disease observed in various animal models. These results demonstrate that phoP mutants are promising new live vaccines for

tuberculosis prevention. The steps that now need to be followed, to take these live vaccines towards clinical trials, are also reviewed, together with the potential of these vaccines to replace BCG.

AB . . . tuberculosis in humans, but this live vaccine confers variable protection against pulmonary tuberculosis in adults. Advances in the understanding of ***Mycobacterium*** tuberculosis immunopathogenesis have renewed hopes of developing new prophylactic vaccines conferring better protection than BCG. The authors describe here state-of-the-art. . .

STP KeyWords Plus (R): ***MYCOBACTERIUM*** -BOVIS BCG; MULTIDRUG-RESISTANT TUBERCULOSIS; BACILLUS-CALMETTE-GUERIN; GUINEA-PIG MODEL; CD8(+) T-CELLS; PROTECTIVE IMMUNITY; PULMONARY TUBERCULOSIS; ENVIRONMENTAL ***MYCOBACTERIA*** ; TRANSPOSON MUTAGENESIS; ***PANTOTHENATE*** ***AUXOTROPH***

L19 ANSWER 10 OF 36 CAPLUS COPYRIGHT 2009 ACS on STN
AN 2007:817460 CAPLUS <<LOGINID::20091103>>
DN 147:210142
TI Use of engineered ***Mycobacterial*** strains comprising SecA2 gene mutations in vaccines for improved immune responses
IN Jacob, William R.; Porcelli, Steven A.; Braunstein, Miriam
PA Albert Einstein College of Medicine of Yeshiva University, USA; The University of North Carolina at Chapel Hill
SO PCT Int. Appl., 65 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2007084353	A2	20070726	WO 2007-US793	20070111
	WO 2007084353	A3	20080110		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
	RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA				
	EP 1981964	A2	20081022	EP 2007-717990	20070111
	R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR				
	IN 2008DN06437	A	20081024	IN 2008-DN6437	20080723
	ZA 2008006387	A	20090429	ZA 2008-6387	20080723
	CN 101395265	A	20090325	CN 2007-80007413	20080901
	US 20090110696	A1	20090430	US 2008-87628	20081204
PRAI	US 2006-758944P	P	20060112		
	WO 2007-US793	W	20070111		

AB The present inventors have discovered that the SecA2 protein prevents host cell apoptosis. The inventors have also discovered that ***mycobacterium*** mutants that do not express SecA2 improve the ability of the ***mycobacterium*** to induce an immune response

against virulent ***mycobacteria*** or recombinant antigens expressed by the ***mycobacteria*** . Thus, the invention is directed to ***mycobacteria*** comprising a mutation in a SecA2 gene, eliminating SecA2 activity. Species of the invention may include M. smegmatis, M. bovis, M. avium, M. phlei, M. fortuitum, M.lufu, M. paratuberculosis, M. habana, M. scrofulaceum, M. intracellulare, M. tuberculosis or M. kansasii. Preferably, the ***mycobacterium*** is a M. bovis BCG or an M. tuberculosis strain useful in vaccines. The ***mycobacterium*** may further comprises a recombinant gene operably linked to a promoter that directs expression of the gene when the ***mycobacterium*** infects a mammalian cell. The gene may encode an antigen, for example of a tumor or most preferably an antigen of a human pathogen to take advantage of the increased immunogenicity to the antigen as a result of the SecA2 gene mutation.

TI Use of engineered ***Mycobacterial*** strains comprising SecA2 gene mutations in vaccines for improved immune responses

AB The present inventors have discovered that the SecA2 protein prevents host cell apoptosis. The inventors have also discovered that ***mycobacterium*** mutants that do not express SecA2 improve the ability of the ***mycobacterium*** to induce an immune response against virulent ***mycobacteria*** or recombinant antigens expressed by the ***mycobacteria*** . Thus, the invention is directed to ***mycobacteria*** comprising a mutation in a SecA2 gene, eliminating SecA2 activity. Species of the invention may include M. smegmatis, M. bovis,. . . M. phlei, M. fortuitum, M.lufu, M. paratuberculosis, M. habana, M. scrofulaceum, M. intracellulare, M. tuberculosis or M. kansasii. Preferably, the ***mycobacterium*** is a M. bovis BCG or an M. tuberculosis strain useful in vaccines. The ***mycobacterium*** may further comprises a recombinant gene operably linked to a promoter that directs expression of the gene when the ***mycobacterium*** infects a mammalian cell. The gene may encode an antigen, for example of a tumor or most preferably an antigen. . .

IT Genetic element
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(***RD1*** , deletion of, in attenuation of ***Mycobacterium*** ; use of engineered ***Mycobacterial*** strains comprising SecA2 gene mutations in vaccines for improved immune responses)

IT Gene, microbial
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(SecA2, ***RD1*** region, deletion of; use of engineered ***Mycobacterial*** strains comprising SecA2 gene mutations in vaccines for improved immune responses)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(SecA2; use of engineered ***Mycobacterial*** strains comprising SecA2 gene mutations in vaccines for improved immune responses)

IT Eubacteria
Virus
(antigen gene expression; use of engineered ***Mycobacterial*** strains comprising SecA2 gene mutations in vaccines for improved immune responses)

IT Amino acids
Vitamins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(***auxotrophy*** for, in attenuation of ***Mycobacterium*** ; use of engineered ***Mycobacterial*** strains comprising SecA2 gene mutations in vaccines for improved immune responses)

IT Parasite
(eukaryote, antigen gene expression; use of engineered ***Mycobacterial*** strains comprising SecA2 gene mutations in vaccines for improved immune responses)
IT Promoter (genetic element)
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(for antigen gene expression; use of engineered ***Mycobacterial*** strains comprising SecA2 gene mutations in vaccines for improved immune responses)
IT Apoptosis
(induction by ***Mycobacterium*** of; use of engineered ***Mycobacterial*** strains comprising SecA2 gene mutations in vaccines for improved immune responses)
IT Animal cell
(mammalian; use of engineered ***Mycobacterial*** strains comprising SecA2 gene mutations in vaccines for improved immune responses)
IT Vaccines
(tumor; use of engineered ***Mycobacterial*** strains comprising SecA2 gene mutations in vaccines for improved immune responses)
IT Genetic engineering
Human
Immunity
Mycobacterium
Mycobacterium BCG
Mycobacterium avium
Mycobacterium avium paratuberculosis
Mycobacterium bovis
Mycobacterium fortuitum
Mycobacterium habana
Mycobacterium intracellulare
Mycobacterium kansasii
Mycobacterium lufu
Mycobacterium phlei
Mycobacterium scrofulaceum
Mycobacterium smegmatis
Mycobacterium tuberculosis
Neoplasm
Vaccines
Virulence (microbial)
(use of engineered ***Mycobacterial*** strains comprising SecA2 gene mutations in vaccines for improved immune responses)
IT Antigens
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of engineered ***Mycobacterial*** strains comprising SecA2 gene mutations in vaccines for improved immune responses)
IT Antitumor agents
(vaccines; use of engineered ***Mycobacterial*** strains comprising SecA2 gene mutations in vaccines for improved immune responses)
IT 944601-37-0 944601-38-1 944601-39-2 944601-40-5 944601-41-6
944601-42-7 944601-43-8 944601-44-9 944601-45-0
RL: PRP (Properties)
(unclaimed nucleotide sequence; use of engineered ***Mycobacterial*** strains comprising SecA2 gene mutations in vaccines for improved immune responses)

IT 138831-86-4
RL: PRP (Properties)
(unclaimed sequence; use of engineered ***Mycobacterial*** strains comprising SecA2 gene mutations in vaccines for improved immune responses)

L19 ANSWER 11 OF 36 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN DUPLICATE 2
AN 2008:47206 BIOSIS <<LOGINID::20091103>>
DN PREV200800049929
TI Failure of a ***Mycobacterium*** tuberculosis Delta ***RD1*** Delta ***panCD*** double deletion mutant in a neonatal calf aerosol M. bovis challenge model: Comparisons to responses elicited by M. bovis bacille Calmette Guerin.
AU Waters, W. Ray [Reprint Author]; Palmer, Mitchell V.; Nonnecke, Brian J.; Thacker, Tyler C.; Scherer, Charles F. Capinos; Estes, D. Mark; Jacobs, William R. Jr.; Glatman-Freedman, Aharona; Larsen, Michelle H.
CS ARS, TB Res Project, Natl Anim Dis Ctr, USDA, 2300 Dayton Ave, Ames, IA 50010 USA
ray.waters@ars.usda.gov
SO Vaccine, (NOV 7 2007) Vol. 25, No. 45, pp. 7832-7840.
CODEN: VACCDE. ISSN: 0264-410X.
DT Article
LA English
ED Entered STN: 4 Jan 2008
Last Updated on STN: 4 Jan 2008
AB An attenuated ***Mycobacterium*** tuberculosis ***RD1*** knockout and ***pantothenate*** ***auxotroph*** (mc(2)6030) vaccine administered at 2 weeks of age failed to protect calves from low dose, aerosol M. bovis challenge at 2.5 months of age. In contrast, M. bovis bacille Calmette Guerin (BCG)-vaccinates had reduced tuberculosis-associated pathology as compared to non- and mc(2)6030-vaccinates. ***Mycobacterial*** colonization was not impacted by vaccination. Positive prognostic indicators associated with reduced pathology in the BCG-vaccinated group were decreased antigen induced IFN-gamma, iNOS, IL-4, and MIP 1-alpha responses, increased antigen induced FoxP3 expression, and a diminished activation phenotype (i.e., down arrow CD25+ and CD44+ cells and up arrow CD62L+ cells) in ***mycobacterial*** -stimulated mononuclear cell cultures. The calf sensitization and challenge model provides an informative screen for candidate tuberculosis vaccines before their evaluation in costly non-human, primates. Published by Elsevier Ltd.
TI Failure of a ***Mycobacterium*** tuberculosis Delta ***RD1*** Delta ***panCD*** double deletion mutant in a neonatal calf aerosol M. bovis challenge model: Comparisons to responses elicited by M. bovis bacille. . .
AB An attenuated ***Mycobacterium*** tuberculosis ***RD1*** knockout and ***pantothenate*** ***auxotroph*** (mc(2)6030) vaccine administered at 2 weeks of age failed to protect calves from low dose, aerosol M. bovis challenge at. . . of age. In contrast, M. bovis bacille Calmette Guerin (BCG)-vaccinates had reduced tuberculosis-associated pathology as compared to non- and mc(2)6030-vaccinates. ***Mycobacterial*** colonization was not impacted by vaccination. Positive prognostic indicators associated with reduced pathology in the BCG-vaccinated group were decreased antigen. . . FoxP3 expression, and a diminished activation phenotype (i.e., down arrow CD25+ and CD44+ cells and up arrow CD62L+ cells) in

mycobacterial -stimulated mononuclear cell cultures. The calf sensitization and challenge model provides an informative screen for candidate tuberculosis vaccines before their evaluation. . .

ORGN . . .
Animalia
Organism Name
bovine (common): newborn, strain-Holstein
Taxa Notes
Animals, Artiodactyls, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Vertebrates
ORGN Classifier
Mycobacteriaceae 08881
Super Taxa
Mycobacteria ; Actinomycetes and Related Organisms; Eubacteria; Bacteria; Microorganisms
Organism Name
Mycobacterium tuberculosis (species)
Mycobacterium bovis (species)
Taxa Notes
Bacteria, Eubacteria, Microorganisms
GEN ***Mycobacterium*** tuberculosis delta- ***RD1*** gene (***Mycobacteriaceae***): mutation; ***Mycobacterium*** tuberculosis delta- ***panCD*** gene (***Mycobacteriaceae***): mutation

L19 ANSWER 12 OF 36 SCISEARCH COPYRIGHT (c) 2009 The Thomson Corporation on STN
AN 2007:1016623 SCISEARCH <<LOGINID::20091103>>
GA The Genuine Article (R) Number: 196JS
TI Enhanced priming of adaptive immunity by a proapoptotic mutant of ***Mycobacterium*** tuberculosis
AU Jacobs, William R., Jr. (Reprint)
CS Yeshiva Univ Albert Einstein Coll Med, Howard Hughes Med Inst, 1300 Morris Pk Ave, Bronx, NY 10461 USA (Reprint)
AU Hinchey, Joseph; Lee, Sunhee; Jeon, Bo Y.; Basaraba, Randall J.; Venkataswamy, Manjunatha M.; Chen, Bing; Chan, John; Braunstein, Miriam; Orme, Ian M.; Derrick, Steven C.; Morris, Sheldon L.; Porcelli, Steven A.
CS Yeshiva Univ Albert Einstein Coll Med, Howard Hughes Med Inst, Bronx, NY 10461 USA; Yeshiva Univ Albert Einstein Coll Med, Dept Microbiol & Immunol, Bronx, NY 10461 USA; US FDA, Ctr Biol Evaluat & Res, Bethesda, MD 20014 USA; Colorado State Univ, Dept Microbiol Immunol & Pathol, Ft Collins, CO 80523 USA; Albert Einstein Coll Med, Dept Med, New York, NY USA; Univ N Carolina, Dept Microbiol, Chapel Hill, NC USA
E-mail: jacobs@aecom.yu.edu; porcelli@aecom.yu.edu
CYA USA
SO JOURNAL OF CLINICAL INVESTIGATION, (AUG 2007) Vol. 117, No. 8, pp. 2279-2288.
ISSN: 0021-9738.
PB AMER SOC CLINICAL INVESTIGATION INC, 35 RESEARCH DR, STE 300, ANN ARBOR, MI 48103 USA.
DT Article; Journal
LA English
REC Reference Count: 47
ED Entered STN: 11 Oct 2007
Last Updated on STN: 11 Oct 2007
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB The inhibition of apoptosis of infected host cells is a well-known but poorly understood function of pathogenic ***mycobacteria*** . We show

that inactivation of the secA2 gene in ***Mycobacterium*** tuberculosis, which encodes a component of a virulence-associated protein secretion system, enhanced the apoptosis of infected macrophages by diminishing secretion of ***mycobacterial*** superoxide dismutase. Deletion of secA2 markedly increased priming of antigen-specific CD8(+) T cells in vivo, and vaccination of mice and guinea pigs with a secA2 mutant significantly increased resistance to M. tuberculosis challenge compared with standard M. bovis bacille Calmette-Guerin vaccination. Our results define a mechanism for a key immune evasion strategy of M. tuberculosis and provide what we believe to be a novel approach for improving ***mycobacterial*** vaccines.

TI Enhanced priming of adaptive immunity by a proapoptotic mutant of ***Mycobacterium*** tuberculosis

AB The inhibition of apoptosis of infected host cells is a well-known but poorly understood function of pathogenic ***mycobacteria*** . We show that inactivation of the secA2 gene in ***Mycobacterium*** tuberculosis, which encodes a component of a virulence-associated protein secretion system, enhanced the apoptosis of infected macrophages by diminishing secretion of ***mycobacterial*** superoxide dismutase. Deletion of secA2 markedly increased priming of antigen-specific CD8(+) T cells in vivo, and vaccination of mice and. . . a key immune evasion strategy of M. tuberculosis and provide what we believe to be a novel approach for improving ***mycobacterial*** vaccines.

STP KeyWords Plus (R): CD8 T-CELLS; BACILLUS-CALMETTE-GUERIN; SUPEROXIDE-DISMUTASE; PATHOGENIC ***MYCOBACTERIA*** ; ***PANTOTHENATE*** ***AUXOTROPH*** ; ANTIMICROBIAL ACTIVITY; MACROPHAGE APOPTOSIS; DNA VACCINE; INFECTION; EXPRESSION

L19 ANSWER 13 OF 36 SCISEARCH COPYRIGHT (c) 2009 The Thomson Corporation on STN

AN 2007:516048 SCISEARCH <<LOGINID::20091103>>

GA The Genuine Article (R) Number: 158MM

TI Vaccine efficacy of an attenuated but persistent ***Mycobacterium*** tuberculosis cysH mutant

AU Bertozzi, Carolyn R. (Reprint)

CS Univ Calif Berkeley, Dept Chem, Berkeley, CA 94720 USA (Reprint)

AU Senaratne, Ryan H.; Mougous, Joseph D.; Reader, J. Rachel; Williams, Spencer J.; Zhang, Tianjiao; Riley, Lee W.

CS Univ Calif Berkeley, Sch Publ Hlth, Berkeley, CA 94720 USA; Univ Calif Davis, Sch Vet Med, Comparat Pathol Lab, Davis, CA 95616 USA; Univ Calif Berkeley, Dept Mol & Cell Biol, Berkeley, CA 94720 USA; Univ Calif Berkeley, Howard Hughes Med Inst, Berkeley, CA 94720 USA
E-mail: crb@berkeley.edu; lwriley@berkeley.edu

CYA USA

SO JOURNAL OF MEDICAL MICROBIOLOGY, (APR 2007) Vol. 56, No. 4, pp. 454-458. ISSN: 0022-2615.

PB SOC GENERAL MICROBIOLOGY, MARLBOROUGH HOUSE, BASINGSTOKE RD, SPENCERS WOODS, READING RG7 1AG, BERKS, ENGLAND.

DT Article; Journal

LA English

REC Reference Count: 16

ED Entered STN: 31 May 2007
Last Updated on STN: 31 May 2007

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The emergence of drug-resistant ***Mycobacterium*** tuberculosis strains and the widespread occurrence of AIDS demand newer and more efficient control of tuberculosis. The protective efficacy of the current

Mycobacterium bovis bacille Calmette-Guerin (BCG) vaccine is highly variable. Therefore, development of an effective new vaccine has gained momentum in recent years. Recently, several M. tuberculosis mutants were tested as potential vaccine candidates in the mouse model of tuberculosis. However, only some of these mutants were able to generate protection equivalent to that of BCG in mice. This study reports the vaccine potential of an attenuated 5'-adenosine phosphosulfate reductase mutant (Delta cysH) of M. tuberculosis. Immunization of mice with either BCG or Delta cysH followed by infection with the virulent M. tuberculosis Erdman strain demonstrated that Delta cysH can generate protection equivalent to that of the BCG vaccine.

TI Vaccine efficacy of an attenuated but persistent ***Mycobacterium*** tuberculosis cysH mutant

AB The emergence of drug-resistant ***Mycobacterium*** tuberculosis strains and the widespread occurrence of AIDS demand newer and more efficient control of tuberculosis. The protective efficacy of the current ***Mycobacterium*** bovis bacille Calmette-Guerin (BCG) vaccine is highly variable. Therefore, development of an effective new vaccine has gained momentum in recent. . .

STP KeyWords Plus (R): CALMETTE-GUERIN INFECTION; ***PANTOTHENATE*** ***AUXOTROPH*** ; RESISTANT TUBERCULOSIS; PROTECTION; BCG; LEUCINE; LYSINE; MICE

L19 ANSWER 14 OF 36 SCISEARCH COPYRIGHT (c) 2009 The Thomson Corporation on STN

AN 2007:736198 SCISEARCH <<LOGINID::20091103>>

GA The Genuine Article (R) Number: 178VK

TI Next generation: Tuberculosis vaccines that elicit protective CD8(+) T cells

AU Behar, Samuel M. (Reprint)

CS Brigham & Womens Hosp, Smith Bldg Room 516C, 1 Jimmy Fund Way, Boston, MA 02115 USA (Reprint)

AU Woodworth, Joshua S. M.; Wu, Ying

CS Brigham & Womens Hosp, Boston, MA 02115 USA; Harvard Univ, Sch Med, Div Rheumatol Allergy & Immunol, Boston, MA 02115 USA

E-mail: sbehar@rics.bwh.harvard.edu

CYA USA

SO EXPERT REVIEW OF VACCINES, (JUN 2007) Vol. 6, No. 3, pp. 441-456. ISSN: 1476-0584.

PB FUTURE DRUGS LTD, UNITEC HOUSE, 3RD FL, 2 ALBERT PLACE, FINCHLEY CENTRAL, LONDON N3 1QB, ENGLAND.

DT General Review; Journal

LA English

REC Reference Count: 111

ED Entered STN: 9 Aug 2007

Last Updated on STN: 9 Aug 2007

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Tuberculosis continues to cause considerable human morbidity and mortality worldwide, particularly in people coinfected with HIV. The emergence of multidrug resistance makes the medical treatment of tuberculosis even more difficult. Thus, the development of a tuberculosis vaccine is a global health priority. Here we review the data concerning the role of CD8(+) T cells in immunity to tuberculosis and consider how CD8(+) T cells can be elicited by vaccination. Many immunization strategies have the potential to elicit CD8+ T cells and we critically review the data supporting a role for vaccine-induced CD8(+) T cells in protective immunity. The synergy between CD4(+) and CD8(+) T cells

suggests that a vaccine that elicits both T-cell subsets has the best chance at preventing tuberculosis.

STP KeyWords Plus (R): BACILLE CALMETTE-GUERIN; ***MYCOBACTERIUM*** -BOVIS BCG; EXPRESSING ANTIGEN 85A; HUMAN DENDRITIC CELLS; PLASMID DNA; VIRUS ANKARA; ENHANCED IMMUNOGENICITY; PULMONARY TUBERCULOSIS; ***PANTOTHENATE*** ***AUXOTROPH*** ; LISTERIA-MONOCYTOGENES

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AN 2007:108973 SCISEARCH <<LOGINID::20091103>>

GA The Genuine Article (R) Number: 122PP

TI Characterization of the protective T-cell response generated in CD4-deficient mice by a live attenuated ***Mycobacterium*** tuberculosis vaccine

AU Derrick, Steven C. (Reprint)

CS NINCDS, Ctr Biol Evaluat & Res, Bldg 10, Bethesda, MD 20892 USA (Reprint)

AU Evering, Teresa H.; Sambandamurthy, Vasan K.; Jalapathy, Kripa V.; Hsu, Tsungda; Chen, Bing; Chen, Mei; Russell, Robert G.; Junqueira-Kipnis, Ana Paula; Orme, Ian M.; Porcelli, Steven A.; Jacobs, William R., Jr.; Morris, Sheldon L.

CS NINCDS, Ctr Biol Evaluat & Res, Bethesda, MD 20892 USA; Albert Einstein Coll Med, Dept Microbiol & Immunol, Bronx, NY 10467 USA; Howard Hughes Med Inst, Chevy Chase, MD USA; Georgetown Univ, Lombardi Canc Ctr, Dept Pathol, Washington, DC 20007 USA; Colorado State Univ, Dept Microbiol Immunol & Pathol, Ft Collins, CO 80523 USA

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CYA USA

SO IMMUNOLOGY, (FEB 2007) Vol. 120, No. 2, pp. 192-206.
ISSN: 0019-2805.

PB BLACKWELL PUBLISHING, 9600 GARSINGTON RD, OXFORD OX4 2DQ, OXON, ENGLAND.

DT Article; Journal

LA English

REC Reference Count: 48

ED Entered STN: 1 Feb 2007
Last Updated on STN: 1 Feb 2007

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The global epidemic of tuberculosis, fuelled by acquired immune-deficiency syndrome, necessitates the development of a safe and effective vaccine. We have constructed a Delta ***RD1*** Delta ***panCD*** mutant of ***Mycobacterium*** tuberculosis (mc(2)6030) that undergoes limited replication and is severely attenuated in immunocompromised mice, yet induces significant protection against tuberculosis in wild-type mice and even in mice that completely lack CD4(+) T cells as a result of targeted disruption of their CD4 genes (CD4(-/-) mice). Ex vivo studies of T cells from mc(2)6030-immunized mice showed that these immune cells responded to protein antigens of M. tuberculosis in a major histocompatibility complex (MHC) class II-restricted manner. Antibody depletion experiments showed that antituberculosis protective responses in the lung were not diminished by removal of CD8(+), T-cell receptor gamma delta (TCR-gamma delta(+)) and NK1.1(+) T cells from vaccinated CD4(-/-) mice before challenge, implying that the observed recall and immune effector functions resulting from vaccination of CD4(-/-) mice with mc(2)6030 were attributable to a population of CD4(-) CD8(-) (double-negative) TCR-alpha beta(+), TCR-gamma delta(-), NK1.1(-) T cells. Transfer of highly enriched double-negative TCR-alpha beta(+) T cells from mc(2)6030-immunized CD4(-/-) mice into naive CD4(-/-) mice resulted in significant protection against an aerosol

tuberculosis challenge. Enriched pulmonary double-negative T cells transcribed significantly more interferon-gamma and interleukin-2 mRNA than double-negative T cells from naive mice after a tuberculous challenge. These results confirmed previous findings on the potential for a subset of MHC class II-restricted T cells to develop and function without expression of CD4 and suggest novel vaccination strategies to assist in the control of tuberculosis in human immunodeficiency virus-infected humans who have chronic depletion of their CD4(+) T cells.

TI Characterization of the protective T-cell response generated in CD4-deficient mice by a live attenuated ***Mycobacterium*** tuberculosis vaccine

AB . . . tuberculosis, fuelled by acquired immune-deficiency syndrome, necessitates the development of a safe and effective vaccine. We have constructed a Delta ***RD1*** Delta ***panCD*** mutant of ***Mycobacterium*** tuberculosis (mc(2)6030) that undergoes limited replication and is severely attenuated in immunocompromised mice, yet induces significant protection against tuberculosis in. . .

STP KeyWords Plus (R): INTRACELLULARE COMPLEX INFECTION; ***PANTOTHENATE*** ***AUXOTROPH*** ; PULMONARY TUBERCULOSIS; ANTIGEN PRESENTATION; CD8-T-CELL MEMORY; CD4-T-CELL HELP; CALMETTE-GUERIN; BOVIS BCG; CD4; LYMPHOCYTES

L19 ANSWER 16 OF 36 CAPLUS COPYRIGHT 2009 ACS on STN

AN 2006:707499 CAPLUS <<LOGINID::20091103>>

DN 145:141111

TI Genes of ***Mycobacterium*** affecting host cell apoptosis and strains with mutations in these genes

IN Jacobs, William R., Jr.; Porcelli, Steven A.; Briken, Volker; Braunstein, Miriam

PA Albert Einstein College of Medicine, USA

SO PCT Int. Appl., 82 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2006076519	A2	20060720	WO 2006-US1132	20060112
	WO 2006076519	A3	20081211		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA				
	AU 2006204907	A1	20060720	AU 2006-204907	20060112
	CA 2597698	A1	20060720	CA 2006-2597698	20060112
	EP 1846024	A2	20071024	EP 2006-733693	20060112
	R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU				

PRAI US 2005-643614P P 20050112
WO 2006-US1132 W 20060112

AB Two genes of ***Mycobacterium*** playing role in the induction of apoptosis in host cells are identified and mutant alleles defective in the induction of apoptosis are generated. The two genes, nlaA and nuoG, are characterized, as are their gene products. Mutation in these genes attenuates the virulence of the bacterium and such attenuated strains may be useful in vaccines. The genes were identified in a screen for genes of ***Mycobacterium*** tuberculosis encoding secreted proteins using an alk. phosphatase reporter technol. Strains deleted in these genes grew slowly in the lungs and spleen of mice when compared to a wild-type strain. Lesions induced by the deletion strains were fewer and smaller than those of control strains. The deletion mutants were immunogenic and induced a stronger immune response than control strains. Mice inoculated with an nlaA deletion strain were able to attenuate a challenge infection with a wild-type M. tuberculosis.

TI Genes of ***Mycobacterium*** affecting host cell apoptosis and strains with mutations in these genes

AB Two genes of ***Mycobacterium*** playing role in the induction of apoptosis in host cells are identified and mutant alleles defective in the induction of. . . bacterium and such attenuated strains may be useful in vaccines. The genes were identified in a screen for genes of ***Mycobacterium*** tuberculosis encoding secreted proteins using an alk. phosphatase reporter technol. Strains deleted in these genes grew slowly in the lungs. . .

ST ***Mycobacterium*** nlaA nuoG apoptosis virulence attenuation vaccine

IT Vaccines
(***Mycobacterium*** , attenuated bacteria for; genes of ***Mycobacterium*** affecting host cell apoptosis and strains with mutations in these genes)

IT Genetic element
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(***RD1*** , deletion in, in attenuation of ***Mycobacterium*** ; genes of ***Mycobacterium*** affecting host cell apoptosis and strains with mutations in these genes)

IT Antigens
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(attenuated ***Mycobacterium*** for vaccine delivery of; genes of ***Mycobacterium*** affecting host cell apoptosis and strains with mutations in these genes)

IT ***Mycobacterium*** BCG
Mycobacterium avium
Mycobacterium avium paratuberculosis
Mycobacterium bovis
Mycobacterium fortuitum
Mycobacterium habana
Mycobacterium intracellulare
Mycobacterium kansasii
Mycobacterium lufu
Mycobacterium phlei
Mycobacterium scrofulaceum
Mycobacterium smegmatis
(attenuation of; genes of ***Mycobacterium*** affecting host cell apoptosis and strains with mutations in these genes)

IT Amino acids
Vitamins
RL: BSU (Biological study, unclassified); BIOL (Biological study)

(***auxotrophy*** for, in attenuation of ***Mycobacterium*** ; genes of ***Mycobacterium*** affecting host cell apoptosis and strains with mutations in these genes)

IT Mutation
(deletion, in attenuation of ***Mycobacterium*** ; genes of ***Mycobacterium*** affecting host cell apoptosis and strains with mutations in these genes)

IT Animal virus
Parasite
Pathogenic bacteria
(genes for antigens of, attenuated ***Mycobacterium*** for vaccine delivery of; genes of ***Mycobacterium*** affecting host cell apoptosis and strains with mutations in these genes)

IT Human
Molecular cloning
Mycobacterium
Mycobacterium tuberculosis
(genes of ***Mycobacterium*** affecting host cell apoptosis and strains with mutations in these genes)

IT Apoptosis
(induction by ***Mycobacterium*** of; genes of ***Mycobacterium*** affecting host cell apoptosis and strains with mutations in these genes)

IT Macrophage
(induction of apoptosis in, by ***Mycobacterium*** ; genes of ***Mycobacterium*** affecting host cell apoptosis and strains with mutations in these genes)

IT Gene, microbial
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nlaA; genes of ***Mycobacterium*** affecting host cell apoptosis and strains with mutations in these genes)

IT Gene, microbial
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nuoG; genes of ***Mycobacterium*** affecting host cell apoptosis and strains with mutations in these genes)

IT Virulence (microbial)
(of ***Mycobacterium*** , attenuation of; genes of ***Mycobacterium*** affecting host cell apoptosis and strains with mutations in these genes)

IT Protein sequences
(of nlaA and nuoG gene products of ***Mycobacterium*** ; genes of ***Mycobacterium*** affecting host cell apoptosis and strains with mutations in these genes)

IT DNA sequences
(of nlaA and nuoG genes of ***Mycobacterium*** ; genes of ***Mycobacterium*** affecting host cell apoptosis and strains with mutations in these genes)

IT 899465-58-8 899465-59-9
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amino acid sequence; genes of ***Mycobacterium*** affecting host cell apoptosis and strains with mutations in these genes)

IT 899465-60-2 899465-61-3
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(nucleotide sequence; genes of ***Mycobacterium*** affecting host cell apoptosis and strains with mutations in these genes)
IT 899465-63-5
RL: PRP (Properties)
(unclaimed nucleotide sequence; genes of ***Mycobacterium*** affecting host cell apoptosis and strains with mutations in these genes)
IT 899465-62-4
RL: PRP (Properties)
(unclaimed protein sequence; genes of ***Mycobacterium*** affecting host cell apoptosis and strains with mutations in these genes)

L19 ANSWER 17 OF 36 SCISEARCH COPYRIGHT (c) 2009 The Thomson Corporation on STN
AN 2006:1074555 SCISEARCH <<LOGINID::20091103>>
GA The Genuine Article (R) Number: 099NA
TI Protection elicited by two glutamine ***auxotrophs*** of ***Mycobacterium*** tuberculosis and in vivo growth phenotypes of the four unique glutamine synthetase mutants in a murine model
AU Jacobs, William R., Jr. (Reprint)
CS Albert Einstein Coll Med, Howard Hughes Med Inst, 1300 Morris Pk Ave, Bronx, NY 10461 USA (Reprint)
AU Lee, Sunhee; Jeon, Bo-Young; Bardarov, Svetoslav; Chen, Mei; Morris, Sheldon L.
CS Albert Einstein Coll Med, Howard Hughes Med Inst, Bronx, NY 10461 USA; Albert Einstein Coll Med, Dept Microbiol & Immunol, Bronx, NY 10461 USA; US FDA, Ctr Biol Evaluat & Res, Bethesda, MD 20014 USA; Univ Massachusetts, Dept Pathol, Worcester, MA 01605 USA
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CYA USA
SO INFECTION AND IMMUNITY, (NOV 2006) Vol. 74, No. 11, pp. 6491-6495.
ISSN: 0019-9567.
PB AMER SOC MICROBIOLOGY, 1752 N ST NW, WASHINGTON, DC 20036-2904 USA.
DT Article; Journal
LA English
REC Reference Count: 27
ED Entered STN: 16 Nov 2006
Last Updated on STN: 16 Nov 2006
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB We generated four individual glutamine synthetase (GS) mutants (Delta gInA1, Delta glnA2, Delta glnA3, and Delta glnA4) and one triple mutant (Delta glnAIEA2) of ***Mycobacterium*** tuberculosis to investigate the roles of GS enzymes. Subcutaneous immunization with the Delta glnA1EA2 and Delta glnA1 glutamine ***auxotrophic*** mutants conferred protection on C57BL/6 mice against an aerosol challenge with virulent M. tuberculosis, which was comparable to that provided by ***Mycobacterium*** bovis BCG vaccination.
TI Protection elicited by two glutamine ***auxotrophs*** of ***Mycobacterium*** tuberculosis and in vivo growth phenotypes of the four unique glutamine synthetase mutants in a murine model
AB . . . glutamine synthetase (GS) mutants (Delta gInA1, Delta glnA2, Delta glnA3, and Delta glnA4) and one triple mutant (Delta glnAIEA2) of ***Mycobacterium*** tuberculosis to investigate the roles of GS enzymes.
Subcutaneous immunization with the Delta glnA1EA2 and Delta glnA1 glutamine ***auxotrophic*** mutants conferred protection on C57BL/6 mice against an aerosol challenge with virulent M. tuberculosis, which was

comparable to that provided by ***Mycobacterium*** bovis BCG vaccination.

STP KeyWords Plus (R): STREPTOMYCES-COELICOLOR A3(2); ***PANTOTHENATE*** ***AUXOTROPH*** ; GUINEA-PIGS; BOVIS BCG; GENE; LEUCINE; EFFICACY; VACCINES; LYSINE; GLNA1

L19 ANSWER 18 OF 36 SCISEARCH COPYRIGHT (c) 2009 The Thomson Corporation on STN

AN 2006:955923 SCISEARCH <<LOGINID::20091103>>

GA The Genuine Article (R) Number: 086VX

TI ***Mycobacterium*** tuberculosis Delta ***RD1*** Delta ***panCD*** : A safe and limited replicating mutant strain that protects immunocompetent and immunocompromised mice against experimental tuberculosis

AU Sambandamurthy V K (Reprint); Derrick S C; Hsu T; Chen B; Larsen M H; Jalapathy K V; Chen M; Kim J; Porcelli S A; Chan J; Morris S L; Jacobs W R

CS US FDA, Ctr Biol Evaluat & Res, Bethesda, MD 20892 USA; Albert Einstein Coll Med, Dept Microbiol & Immunol, Bronx, NY 10461 USA; Albert Einstein Coll Med, Dept Med, Bronx, NY 10461 USA; Novartis Inst Trop Dis, Singapore 138670, Singapore
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CYA USA; Singapore

SO VACCINE, (11 SEP 2006) Vol. 24, No. 37-39, pp. 6309-6320.
ISSN: 0264-410X.

PB ELSEVIER SCI LTD, THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD OX5 1GB, OXON, ENGLAND.

DT Article; Journal

LA English

REC Reference Count: 40

ED Entered STN: 18 Oct 2006
Last Updated on STN: 18 Oct 2006
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The global epidemic of tuberculosis (TB), fueled by the growing HIV pandemic, warrants the development of a safe and effective vaccine against TB. We report the construction and characterization of an unlinked double deletion mutant of ***Mycobacterium*** tuberculosis H37Rv that deletes both the primary attenuating mutation of BCG (Delta ***RD1***) and two genes required for the synthesis of ***pantothenate*** (Delta ***panCD***). The M. tuberculosis Delta ***RD1*** Delta ***panCD*** (mc(2)6030) mutant undergoes limited replication in mice, and yet is both significantly safer than BCG in immunocompromised mice and also safe in guinea pigs. Additionally, the mc(2)6030 strain does not reactivate in a mouse chemo-immunosuppression model. Importantly, long-lived protective immune responses following immunization with the mc(2)6030 strain prolong the survival of wild type mice, and CD4-deficient mice against an aerosol challenge with virulent M. tuberculosis. Given its overall safety and effectiveness, the mc(2)6030 live attenuated strain should be considered as a human vaccine candidate for protecting both healthy and HIV-infected individuals against TB. (c) 2006 Elsevier Ltd. All rights reserved.

TI ***Mycobacterium*** tuberculosis Delta ***RD1*** Delta ***panCD*** : A safe and limited replicating mutant strain that protects immunocompetent and immunocompromised mice against experimental tuberculosis

AB . . . a safe and effective vaccine against TB. We report the construction and characterization of an unlinked double deletion mutant of ***Mycobacterium*** tuberculosis H37Rv that deletes both the primary

attenuating mutation of BCG (Delta ***RD1***) and two genes required for the synthesis of ***pantothenate*** (Delta ***panCD***). The M. tuberculosis Delta ***RD1*** Delta ***panCD*** (mc(2)6030) mutant undergoes limited replication in mice, and yet is both significantly safer than BCG in immunocompromised mice and also. . .

ST Author Keywords: tuberculosis; ***mycobacterial*** vaccines; BCG; attenuated strains

STP KeyWords Plus (R): BACILLUS-CALMETTE-GUERIN; T-CELL SUBSETS; BOVIS BCG; ***PANTOTHENATE*** ***AUXOTROPH*** ; INTERFERON-GAMMA; IN-VITRO; IMMUNODEFICIENT MICE; IMMUNE-RESPONSE; INFECTION; VACCINES

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AN 2006:477195 SCISEARCH <<LOGINID::20091103>>

GA The Genuine Article (R) Number: 035MM

TI The live ***Mycobacterium*** tuberculosis phoP mutant strain is more attenuated than BCG and confers protective immunity against tuberculosis in mice and guinea pigs

AU Martin C (Reprint)

CS Univ Zaragoza, Fac Med, Dept Microbiol, Grp Genet Micobacterias, E-50009 Zaragoza, Spain (Reprint)

AU Williams A; Hernandez-Pando R; Cardona P J; Gormley E; Bordat Y; Soto C Y; Clark S O; Hatch G J; Aguilar D; Ausina V; Gicquel B

CS Hlth Protect Agcy, Salisbury SP4 0JG, Wilts, England; Natl Inst Med Sci & Nutr Salvador Zubiran, Dept Pathol, Expt Pathol Sect, Mexico City, DF, Mexico; Autonomous Univ Barcelona, Fdn Inst Invest Ciencies Salut Germans Trias & Pu, Serv Microbiol, Unitat TB Expt, E-08193 Barcelona, Spain; Univ Coll Dublin, Sch Agr Food Sci & Vet Med, Dublin 2, Ireland; Inst Pasteur, Unite Genet Mycobacterienne, Paris, France

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CYA Spain; England; Mexico; Ireland; France

SO VACCINE, (24 APR 2006) Vol. 24, No. 17, pp. 3408-3419.
ISSN: 0264-410X.

PB ELSEVIER SCI LTD, THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD OX5 1GB, OXON, ENGLAND.

DT Article; Journal

LA English

REC Reference Count: 40

ED Entered STN: 18 May 2006
Last Updated on STN: 18 May 2006

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The ***Mycobacterium*** tuberculosis phoP mutant strain SO2 has previously been shown to have reduced multiplication in mouse macrophages and in vivo using the mouse intravenous-infection model. In this study we demonstrate that the M. tuberculosis SO2 is highly attenuated when compared with the parental M. tuberculosis MT103 strain and also more attenuated than BCG in severe combined immunodeficiency disease (SCID) mice. Complementation of the M. tuberculosis SO2 with the wild-type phoP gene restored the virulence of the strain in the SCID mice, confirming that the attenuated phenotype is due to the phoP mutation. In Balb/c mice subcutaneously vaccinated with either M. tuberculosis SO2 or BCG, the proportions of CD4(+) and CD8(+) populations measured in the spleen were significantly higher in the M. tuberculosis SO2 vaccinated group. In addition, the proportion of antigen-stimulated CD4(+)/CD8(+) cells

expressing IFN-gamma was significantly higher in the M. tuberculosis SO2 vaccinated group when compared with the BCG group. Balb/c mice subcutaneously vaccinated with the M. tuberculosis SO2 strain were also protected against intra-venous challenge with M. tuberculosis H37Rv at levels comparable to mice vaccinated with BCG, as measured by reduced bacterial counts in lung and spleens. Guinea pigs subcutaneously vaccinated with the M. tuberculosis SO2 strain were protected against aerosol challenge with M. tuberculosis H37Rv delivered at different doses. A high dose aerosol challenge of M. tuberculosis SO2 vaccinated guinea pigs resulted in superior levels of protection when compared with BCG vaccination, as measured by guinea pig survival and reduction in disease severity in the lung.

TI The live ***Mycobacterium*** tuberculosis phoP mutant strain is more attenuated than BCG and confers protective immunity against tuberculosis in mice and guinea pigs

AB The ***Mycobacterium*** tuberculosis phoP mutant strain SO2 has previously been shown to have reduced multiplication in mouse macrophages and in vivo using. . .

STP KeyWords Plus (R): TRANSPOSON MUTAGENESIS; PULMONARY TUBERCULOSIS; ***PANTOTHENATE*** ***AUXOTROPH*** ; VIRULENCE GENE; VACCINES; MODEL; SYSTEM; BOVIS; VACCINATION; RESISTANCE

L19 ANSWER 20 OF 36 SCISEARCH COPYRIGHT (c) 2009 The Thomson Corporation on STN

AN 2006:352695 SCISEARCH <<LOGINID::20091103>>

GA The Genuine Article (R) Number: 028HF

TI Evaluation of the Mtb72F polyprotein vaccine in a rabbit model of tuberculous meningitis

AU Kaplan G (Reprint)

CS Publ Hlth Res Inst, Lab Mycobacterial Immun & Pathogenesis, 225 Warren St, Newark, NJ 07103 USA (Reprint)

AU Tsenova L; Harbacheuski R; Moreira A L; Ellison E; Dalemans W; Alderson M R; Mathema B; Reed S G; Skeiky Y A W

CS Publ Hlth Res Inst, Lab Mycobacterial Immun & Pathogenesis, Newark, NJ 07103 USA; Publ Hlth Res Inst, Tuberculosis Ctr, Newark, NJ 07103 USA; Mem Sloan Kettering Canc Ctr, New York, NY 10021 USA; GlaxoSmithKline Biol, Rixensart, Belgium; Corixa Corp, Seattle, WA 98104 USA; Infect Dis Res Inst, Seattle, WA 98104 USA; Columbia Univ, Mailman Sch Publ Hlth, Dept Epidemiol, New York, NY 10032 USA

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CYA USA; Belgium

SO INFECTION AND IMMUNITY, (APR 2006) Vol. 74, No. 4, pp. 2392-2401. ISSN: 0019-9567.

PB AMER SOC MICROBIOLOGY, 1752 N ST NW, WASHINGTON, DC 20036-2904 USA.

DT Article; Journal

LA English

REC Reference Count: 49

ED Entered STN: 13 Apr 2006
Last Updated on STN: 13 Apr 2006

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Using a rabbit model of tuberculous meningitis, we evaluated the protective efficacy of vaccination with the recombinant polyprotein Mtb72F, which is formulated in two alternative adjuvants, AS02A and AS01B, and compared this to vaccination with ***Mycobacterium*** bovis bacillus Calmette-Guerin (BCG) alone or as a BCG prime/Mtb72F-boost regimen. Vaccination with Mtb72F formulated in AS02A (Mtb72F+AS02A) or

Mtb72F formulated in AS01B (Mtb72F+AS01B) was protective against central nervous system (CNS) challenge with ***Mycobacterium*** tuberculosis H37Rv to an extent comparable to that of vaccination with BCG. Similar accelerated clearances of bacilli from the cerebrospinal fluid, reduced leukocytosis, and less pathology of the brain and lungs were noted. Weight loss of infected rabbits was less extensive for Mtb72F+AS02A-vaccinated rabbits. In addition, protection against M. tuberculosis H37Rv CNS infection afforded by BCG/Mtb72F in a prime-boost strategy was similar to that by BCG alone. Interestingly, Mtb72F+AS01B induced better protection against leukocytosis and weight loss, suggesting that the polyprotein in this adjuvant may boost immunity without exacerbating inflammation in previously BCG-vaccinated individuals.

AB . . . the recombinant polyprotein Mtb72F, which is formulated in two alternative adjuvants, AS02A and AS01B, and compared this to vaccination with ***Mycobacterium*** bovis bacillus Calmette-Guerin (BCG) alone or as a BCG prime/Mtb72F-boost regimen. Vaccination with Mtb72F formulated in AS02A (Mtb72F+AS02A) or Mtb72F formulated in AS01B (Mtb72F+AS01B) was protective against central nervous system (CNS) challenge with ***Mycobacterium*** tuberculosis H37Rv to an extent comparable to that of vaccination with BCG. Similar accelerated clearances of bacilli from the cerebrospinal. . .

STP KeyWords Plus (R): BOVIS BCG VACCINE; ***MYCOBACTERIUM*** -TUBERCULOSIS; EXPRESSION CLONING; IMMUNOLOGICAL EVALUATION; ***PANTOTHENATE*** ***AUXOTROPH*** ; PROTECTIVE IMMUNITY; GUINEA-PIGS; ANTIGEN; INFECTION; EFFICACY

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AN 2006:718850 SCISEARCH <<LOGINID::20091103>>

GA The Genuine Article (R) Number: 063ND

TI Advances in tuberculosis vaccine strategies

AU Skeiky Y A W (Reprint)

CS Aeras Global TB Vaccine Fdn, 1405 Res Blvd, Rockville, MD 20850 USA (Reprint)

AU Sadoff J C

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CYA USA

SO NATURE REVIEWS MICROBIOLOGY, (JUN 2006) Vol. 4, No. 6, pp. 469-476. ISSN: 1740-1526.

PB NATURE PUBLISHING GROUP, MACMILLAN BUILDING, 4 CRINAN ST, LONDON N1 9XW, ENGLAND.

DT General Review; Journal

LA English

REC Reference Count: 107

ED Entered STN: 3 Aug 2006
Last Updated on STN: 31 Aug 2006

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Tuberculosis (TB), an ancient human scourge, is a growing health problem in the developing world. Approximately two million deaths each year are caused by TB, which is the leading cause of death in HIV-infected individuals. Clearly, an improved TB vaccine is desperately needed. Heterologous prime-boost regimens probably represent the best hope for an improved vaccine regimen to prevent TB. This first generation of new vaccines might also complement drug treatment regimens and be effective against reactivation of TB from the latent state, which would significantly enhance their usefulness.

STP KeyWords Plus (R): ***MYCOBACTERIUM*** -BOVIS BCG; GUINEA-PIG MODEL; IMMUNODEFICIENCY-VIRUS-INFECTION; T-CELL ANTIGENS; PROTECTIVE EFFICACY; INTERFERON-GAMMA; SUBUNIT VACCINE; PULMONARY TUBERCULOSIS; ***PANTOTHENATE*** ***AUXOTROPH*** ; EFFICIENT PROTECTION

L19 ANSWER 22 OF 36 SCISEARCH COPYRIGHT (c) 2009 The Thomson Corporation on STN
AN 2006:561801 SCISEARCH <<LOGINID::20091103>>
GA The Genuine Article (R) Number: 047GX
TI The use of mutant ***mycobacteria*** as new vaccines to prevent tuberculosis
AU Pando R H (Reprint)
CS Inst Nacl Nutr Salvador Zubiran, Dept Pathol, Expt Pathol Sect, Vasco Quiroga 15, Mexico City 14000, DF, Mexico (Reprint)
AU Aguilar L D; Infante E; Cataldi A; Bigi F; Martin C; Gicquel B
CS Inst Nacl Nutr Salvador Zubiran, Dept Pathol, Expt Pathol Sect, Mexico City 14000, DF, Mexico; INTA, CICVyA, Inst Biotechnol, Castelar, Argentina; Univ Zaragoza, Dept Microbiol, Mycobacteria Genet Grp, E-50009 Zaragoza, Spain; Inst Pasteur, Unite Genet Mycobacterienne, Paris, France
E-mail: rhpando@quetzal.innsz.mx
CYA Mexico; Argentina; Spain; France
SO TUBERCULOSIS, (MAY-JUL 2006) Vol. 86, No. 3-4, pp. 203-210.
ISSN: 1472-9792.
PB CHURCHILL LIVINGSTONE, JOURNAL PRODUCTION DEPT, ROBERT STEVENSON HOUSE, 1-3 BAXTERS PLACE, LEITH WALK, EDINBURGH EH1 3AF, MIDLOTHIAN, SCOTLAND.
DT Article; Journal
LA English
REC Reference Count: 59
ED Entered STN: 15 Jun 2006
Last Updated on STN: 15 Jun 2006
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Given the variable protective efficacy generated by ***Mycobacterium*** bovis BCG (Bacillus Calmette-Guerin), there is a concerted effort worldwide to develop better vaccines that could be used to reduce the burden of tuberculosis. Rational attenuated mutants of ***Mycobacterium*** tuberculosis are vaccine candidates that offer some potential in this area. In this paper, we will discuss the molecular methods used to generate mutant ***mycobacteria*** , as well as the results obtained with some of these strains, in terms of attenuation, immunogenicity and level of protection, when compared with the conventional BCG vaccine in diverse animal models. Tuberculosis vaccine candidates based on safe and live ***mycobacterial*** mutants could be promising candidates. (c) 2006 Elsevier Ltd. All rights reserved.
TI The use of mutant ***mycobacteria*** as new vaccines to prevent tuberculosis
AB Given the variable protective efficacy generated by ***Mycobacterium*** bovis BCG (Bacillus Calmette-Guerin), there is a concerted effort worldwide to develop better vaccines that could be used to reduce the burden of tuberculosis. Rational attenuated mutants of ***Mycobacterium*** tuberculosis are vaccine candidates that offer some potential in this area. In this paper, we will discuss the molecular methods used to generate mutant ***mycobacteria*** , as well as the results obtained with some of these strains, in terms of attenuation, immunogenicity and level of protection, when compared with the conventional BCG vaccine in diverse animal models. Tuberculosis vaccine candidates based on safe and live ***mycobacterial*** mutants could be promising candidates. (c) 2006 Elsevier Ltd. All rights reserved.

ST Author Keywords: ***mycobacterial*** mutants; ***Mycobacterium*** tuberculosis
STP KeyWords Plus (R): BOVIS BCG; IMMUNE-RESPONSE; TRANSPOSON MUTAGENESIS; PULMONARY TUBERCULOSIS; ***PANTOTHENATE*** ***AUXOTROPH*** ; PROTECTIVE EFFICACY; ACID BIOSYNTHESIS; GENE REPLACEMENT; VIRULENCE GENE; SMEGMATIS

L19 ANSWER 23 OF 36 CAPLUS COPYRIGHT 2009 ACS on STN
AN 2005:1242628 CAPLUS <<LOGINID::20091103>>
DN 144:5382
TI ***RD1*** region-altered or deleted ***Mycobacterium*** tuberculosis as vaccines for treating tuberculosis in mammal and human
IN Jacobs, William R., Jr.; Bloom, Barry; Hondalus, Mary K.; Sampson, Samantha; Sambandamurthy, Vasan
PA Howard Hughes Medical Institute, USA
SO U.S. Pat. Appl. Publ., 76 pp., Cont.-in-part of U.S. Ser. No. 351,452. CODEN: USXXCO
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 20050260232	A1	20051124	US 2005-109056	20050419
	US 20040001866	A1	20040101	US 2003-351452	20030124
PRAI	US 2002-358152P	P	20020219		
	US 2003-351452	A2	20030124		

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
AB Non-naturally occurring ***mycobacteria*** in the ***Mycobacterium*** tuberculosis complex are provided. These ***mycobacteria*** have a deletion of an ***RD1*** region or a region (e.g. leuD or ***panCD*** genes) controlling prodn. of a vitamin, and exhibit attenuated virulence in a mammal when compared to the ***mycobacteria*** without the deletion. Also provided are non-naturally occurring ***mycobacteria*** that have a deletion of a region controlling prodn. of lysine, and ***mycobacteria*** comprising two attenuating deletions. Vaccines comprising these ***mycobacteria*** are also provided, as are methods of protecting mammals from virulent ***mycobacteria*** using the vaccines. Also provided are methods of prepg. these vaccines which include the step of deleting an ***RD1*** region or a region controlling prodn. of a vitamin or the amino acids leucine and lysine from a ***mycobacterium*** in the M. tuberculosis complex. Embodiments of these ***mycobacteria*** , vaccines and methods, encompassing ***mycobacteria*** comprising a leucine ***auxotrophy*** and a ***pantothenate*** ***auxotrophy*** , are also provided.
TI ***RD1*** region-altered or deleted ***Mycobacterium*** tuberculosis as vaccines for treating tuberculosis in mammal and human
AB Non-naturally occurring ***mycobacteria*** in the ***Mycobacterium*** tuberculosis complex are provided. These ***mycobacteria*** have a deletion of an ***RD1*** region or a region (e.g. leuD or ***panCD*** genes) controlling prodn. of a vitamin, and exhibit attenuated virulence in a mammal when compared to the ***mycobacteria*** without the deletion. Also provided are non-naturally occurring ***mycobacteria*** that have a deletion of a region controlling prodn. of lysine, and ***mycobacteria*** comprising two attenuating deletions. Vaccines comprising these ***mycobacteria*** are also provided, as are methods of protecting mammals from virulent

mycobacteria using the vaccines. Also provided are methods of prepg. these vaccines which include the step of deleting an ***RD1*** region or a region controlling prodn. of a vitamin or the amino acids leucine and lysine from a ***mycobacterium*** in the M. tuberculosis complex. Embodiments of these ***mycobacteria*** , vaccines and methods, encompassing ***mycobacteria*** comprising a leucine ***auxotrophy*** and a ***pantothenate*** ***auxotrophy*** , are also provided.

ST ***RD1*** leuD ***panCD*** gene deletion mutation ***Mycobacterium*** tuberculosis vaccine; leucine lysine ***pantothenate*** vitamin ***auxotrophy*** ***Mycobacterium*** tuberculosis complex vaccine

IT ***Mycobacterium*** tuberculosis
(H37Rv; ***RD1*** region-altered or deleted ***Mycobacterium*** tuberculosis as vaccines for treating tuberculosis in mammal and human)

IT Bos taurus
DNA sequences
Drug delivery systems
Human
Mammalia
Molecular cloning
Mutagenesis
Mycobacterium bovis
Tuberculosis
Vaccines
(***RD1*** region-altered or deleted ***Mycobacterium*** tuberculosis as vaccines for treating tuberculosis in mammal and human)

IT Vitamins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(***RD1*** region-altered or deleted ***Mycobacterium*** tuberculosis as vaccines for treating tuberculosis in mammal and human)

IT Gene, microbial
RL: BSU (Biological study, unclassified); PRP (Properties); REM (Removal or disposal); BIOL (Biological study); PROC (Process)
(***RD1*** ; ***RD1*** region-altered or deleted ***Mycobacterium*** tuberculosis as vaccines for treating tuberculosis in mammal and human)

IT Microorganism
(***auxotrophic*** ; leucine/lysine/ ***pantothenate*** - ***auxotrophic*** ***Mycobacterium*** tuberculosis as vaccines for treating tuberculosis in mammal and human)

IT Gene, microbial
RL: BSU (Biological study, unclassified); PRP (Properties); REM (Removal or disposal); BIOL (Biological study); PROC (Process)
(leuD; ***RD1*** region-altered or deleted ***Mycobacterium*** tuberculosis as vaccines for treating tuberculosis in mammal and human)

IT Gene, microbial
RL: BSU (Biological study, unclassified); PRP (Properties); REM (Removal or disposal); BIOL (Biological study); PROC (Process)
(lysA; ***RD1*** region-altered or deleted ***Mycobacterium*** tuberculosis as vaccines for treating tuberculosis in mammal and human)

IT Gene, microbial
RL: BSU (Biological study, unclassified); PRP (Properties); REM (Removal or disposal); BIOL (Biological study); PROC (Process)
(nadBC; ***RD1*** region-altered or deleted ***Mycobacterium*** tuberculosis as vaccines for treating tuberculosis in mammal and human)

IT Gene, microbial

RL: BSU (Biological study, unclassified); PRP (Properties); REM (Removal or disposal); BIOL (Biological study); PROC (Process)
(***panCD*** ; ***RD1*** region-altered or deleted ***Mycobacterium*** tuberculosis as vaccines for treating tuberculosis in mammal and human)

IT Mutagenesis
(site-directed, deletion; ***RD1*** region-altered or deleted ***Mycobacterium*** tuberculosis as vaccines for treating tuberculosis in mammal and human)

IT 56-87-1, L-Lysine, biological studies 61-90-5, L-Leucine, biological studies 79-83-4
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(***RD1*** region-altered or deleted ***Mycobacterium*** tuberculosis as vaccines for treating tuberculosis in mammal and human)

IT 870107-04-3 870107-05-4 870107-06-5 870107-07-6 870107-08-7
RL: BSU (Biological study, unclassified); PRP (Properties); REM (Removal or disposal); BIOL (Biological study); PROC (Process)
(nucleotide sequence; ***RD1*** region-altered or deleted ***Mycobacterium*** tuberculosis as vaccines for treating tuberculosis in mammal and human)

IT 870109-36-7 870109-37-8 870109-38-9 870109-39-0 870109-40-3 870109-41-4 870109-42-5
RL: PRP (Properties)
(unclaimed nucleotide sequence; ***rD1*** region-altered or deleted ***Mycobacterium*** tuberculosis as vaccines for treating tuberculosis in mammal and human)

L19 ANSWER 24 OF 36 SCISEARCH COPYRIGHT (c) 2009 The Thomson Corporation on STN
AN 2006:36773 SCISEARCH <<LOGINID::20091103>>
GA The Genuine Article (R) Number: 997FM
TI A review of vaccine research and development: Tuberculosis
AU Girard M P (Reprint)
CS Univ Paris 07, UFR Biochem, 39 Seignemartin, F-69008 Lyon, France (Reprint)
AU Fruth U; Kieny M P
CS Univ Paris 07, UFR Biochem, F-69008 Lyon, France; WHO, Initiat Vaccine Res, CH-1211 Geneva, Switzerland
E-mail: marc.girard36@wanadoo.fr; fruthu@who.int; kienym@who.int
CYA France; Switzerland
SO VACCINE, (30 DEC 2005) Vol. 23, No. 50, pp. 5725-5731.
ISSN: 0264-410X.
PB ELSEVIER SCI LTD, THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD OX5 1GB, OXON, ENGLAND.
DT General Review; Journal
LA English
REC Reference Count: 57
ED Entered STN: 11 Jan 2006
Last Updated on STN: 11 Jan 2006
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Substantial progress has been made during the past 15 years towards the development of improved vaccines for tuberculosis. This is due to advances in the characterization of genes and antigens of ***MYcobacterium*** tuberculosis (M. tb), aided by the availability of genome, sequences of different ***mycobacterial*** species and M. tb isolates and to greater understanding of protective immune responses to the pathogen in both animals and humans. More than one hundred candidate

vaccines have been tested in animal models, representing all of the major vaccine design strategies, and some have now moved into clinical trials. This review summarizes recent advances in tuberculosis vaccine development. (c) 2005 Published by Elsevier Ltd.

AB . . . the development of improved vaccines for tuberculosis. This is due to advances in the characterization of genes and antigens of ***MYcobacterium*** tuberculosis (M. tb), aided by the availability of genome, sequences of different ***mycobacterial*** species and M. tb isolates and to greater understanding of protective immune responses to the pathogen in both animals and. . .

STP KeyWords Plus (R): CALMETTE-GUERIN STRAINS; ***MYCOBACTERIUM*** -TUBERCULOSIS; PROTECTIVE IMMUNITY; ***PANTOTHENATE*** ***AUXOTROPH*** ; BOVINE TUBERCULOSIS; SUBUNIT VACCINE; TB VACCINES; DNA VACCINE; BCG VACCINE; INFECTION

L19 ANSWER 25 OF 36 SCISEARCH COPYRIGHT (c) 2009 The Thomson Corporation on STN

AN 2005:603878 SCISEARCH <<LOGINID::20091103>>

GA The Genuine Article (R) Number: 931YT

TI New live ***mycobacterial*** vaccines: the Geneva consensus on essential steps towards clinical development

AU Lambert P H (Reprint)

CS Univ Geneva, Dept Pathol & Immunol, Ctr Vaccinol & Neonatal Immunol, 1 Rue Michel Servet, CH-1211 Geneva, Switzerland (Reprint)

AU Kamath A T; Fruth U L; Brennan M J; Dobbelaer R; Hubrechts P; Ho M M; Mayner R E; Thole J; Walker K B; Liu M

CS Univ Geneva, Dept Pathol & Immunol, Ctr Vaccinol & Neonatal Immunol, CH-1211 Geneva, Switzerland; WHO, Initiat Vaccine Res, CH-1211 Geneva, Switzerland; US FDA, Ctr Biol Evaluat & Res, Bethesda, MD 20014 USA; Sci Inst Publ Hlth, Brussels, Belgium; Statens Serum Inst, Qual Control Dept, DK-2300 Copenhagen, Denmark; Natl Inst Biol Stand & Controls, Div Bacteriol, Potters Bar EN6 3QG, Herts, England; Aeras Global TB Vaccine Fdn, Bethesda, MD USA; Anim Sci Grp, Div Infect Dis, Lelystad, Netherlands; Natl Inst Biol Stand & Controls, Div Immunobiol, Potters Bar EN6 3QG, Herts, England; Transgene SA, Strasbourg, France
E-mail: Paul.Lambert@medecine.unige.ch

CYA Switzerland; USA; Belgium; Denmark; England; Netherlands; France

SO VACCINE, (31 MAY 2005) Vol. 23, No. 29, pp. 3753-3761.
ISSN: 0264-410X.

PB ELSEVIER SCI LTD, THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD OX5 1GB, OXON, ENGLAND.

DT Article; Journal

LA English

REC Reference Count: 21

ED Entered STN: 16 Jun 2005
Last Updated on STN: 16 Jun 2005
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB As the disease caused by ***Mycobacterium*** tuberculosis continues to be a burden, which the world continues to suffer, there is a concerted effort to find new vaccines to combat this problem. Of the various vaccines strategies, one viable option is the development of live ***mycobacterial*** vaccines. A meeting with researchers, regulatory bodies, vaccines developers and manufactures was held to consider the challenges and progress, which has been achieved with live ***mycobacterial*** vaccines (either modified BCG or attenuated M. tuberculosis). Discussion led to the production of a consensus document of the proposed entry criteria for Phase I clinical trials of candidate

live ***mycobacterial*** vaccines. The vaccine must be characterised thoroughly to prove identity and consistency, as clinical trial lots are prepared. In pre-clinical studies, greater protective efficacy as well as improved safety potential relative to BCG should be considered when assessing potential vaccine candidates. A standard way to measure the protective efficacy to facilitate comparison between vaccine candidates was suggested. Additional safety criteria and verification of attenuation must be considered for attenuated M. tuberculosis. Two non-reverting independent mutations are recommended for such vaccines. When entering Phase I trials, enrolment should be based upon an acceptable characterisation of the study population regarding ***mycobacterium*** status and exclude HIV+ individuals. BCG could be used as a comparator for blinding during the trials and to properly assess vaccine-specific adverse reactions, while assays are being developed to assess immunogenicity of vaccines. The proposed criteria suggested in this consensus document may facilitate the movement of the most promising vaccine candidates to the clinic and towards control of tuberculosis. © 2005 Elsevier Ltd. All rights reserved.

TI New live ***mycobacterial*** vaccines: the Geneva consensus on essential steps towards clinical development

AB As the disease caused by ***Mycobacterium*** tuberculosis continues to be a burden, which the world continues to suffer, there is a concerted effort to find new vaccines to combat this problem. Of the various vaccines strategies, one viable option is the development of live ***mycobacterial*** vaccines. A meeting with researchers, regulatory bodies, vaccines developers and manufactures was held to consider the challenges and progress, which has been achieved with live ***mycobacterial*** vaccines (either modified BCG or attenuated M. tuberculosis). Discussion led to the production of a consensus document of the proposed entry criteria for Phase I clinical trials of candidate live ***mycobacterial*** vaccines. The vaccine must be characterised thoroughly to prove identity and consistency, as clinical trial lots are prepared. In pre-clinical. . . such vaccines. When entering Phase I trials, enrolment should be based upon an acceptable characterisation of the study population regarding ***mycobacterium*** status and exclude HIV+ individuals. BCG could be used as a comparator for blinding during the trials and to properly. . .

ST Author Keywords: ***Mycobacterium*** tuberculosis; vaccines; trials

STP KeyWords Plus (R): ***PANTOTHENATE*** ***AUXOTROPH*** ; PUBLISHED LITERATURE; ENHANCED PROTECTION; BCG VACCINES; TUBERCULOSIS; VACCINATION; PREVENTION; VIRULENCE; ANTIGENS; EFFICACY

L19 ANSWER 26 OF 36 SCISEARCH COPYRIGHT (c) 2009 The Thomson Corporation on STN

AN 2006:44957 SCISEARCH <<LOGINID::20091103>>

GA The Genuine Article (R) Number: 998EL

TI Tuberculosis vaccines - Current progress

AU Orme I M (Reprint)

CS Colorado State Univ, Mycobacteria Res Labs, Dept Microbiol Immunol & Pathol, 1682 Campus Delivery, Ft Collins, CO 80523 USA (Reprint)

AU Orme I M (Reprint)

CS Colorado State Univ, Mycobacteria Res Labs, Dept Microbiol Immunol & Pathol, Ft Collins, CO 80523 USA

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CYA USA

SO DRUGS, (2005) Vol. 65, No. 17, pp. 2437-2444.

ISSN: 0012-6667.

PB ADIS INTERNATIONAL LTD, 41 CENTORIAN DR, PRIVATE BAG 65901, MAIRANGI BAY, AUCKLAND 1311, NEW ZEALAND.
DT Article; Journal
LA English
REC Reference Count: 51
ED Entered STN: 19 Jan 2006
Last Updated on STN: 19 Jan 2006
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Tuberculosis continues to be a major cause of disease and death throughout the developing world. Chemotherapy is the current method of control but with the continuing emergence of drug resistance, coupled with the reticence of major drug companies to invest in drug discovery, the identification of new vaccines to combat tuberculosis is a pressing need. Rational vaccine design requires knowledge of the protective immune response and, while this is not fully understood, it is clear that induction of a T-helper-1 type of immunity is critical to host resistance. A variety of animal models, but especially the mouse and guinea pig, can be used to determine the protective efficacy of new vaccines. These mostly consist of relatively short-term prophylactic models in which animals are vaccinated and then challenged by the aerosol infection route to determine their capacity to reduce the lung bacterial load. Several promising vaccine types have emerged, including subunit vaccines, DNA vaccines and vaccines based upon living vectors, such as recombinant bacillus Calmette-Guerin (BCG) vaccines and ***auxotrophic*** or gene disrupted mutants of ***Mycobacterium*** tuberculosis. A few of these have already entered early stage clinical trials.
AB . . . emerged, including subunit vaccines, DNA vaccines and vaccines based upon living vectors, such as recombinant bacillus Calmette-Guerin (BCG) vaccines and ***auxotrophic*** or gene disrupted mutants of ***Mycobacterium*** tuberculosis. A few of these have already entered early stage clinical trials.
STP KeyWords Plus (R): ***MYCOBACTERIUM*** -BOVIS BCG; GUINEA-PIG MODEL; PROTECTIVE EFFICACY; ENHANCED IMMUNOGENICITY; PULMONARY TUBERCULOSIS; ***PANTOTHENATE*** ***AUXOTROPH*** ; SECRETED ANTIGENS; INTERFERON-GAMMA; DNA-VACCINATION; RECOMBINANT BCG

L19 ANSWER 27 OF 36 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN DUPLICATE 3
AN 2005:169360 BIOSIS <<LOGINID::20091103>>
DN PREV200500170314
TI Long-term protection against tuberculosis following vaccination with a severely attenuated double lysine and ***pantothenate*** ***auxotroph*** of ***Mycobacterium*** tuberculosis.
AU Sambandamurthy, Vasan K.; Derrick, Steven C.; Jalapathy, Kripa V.; Chen, Bing; Russell, Robert G.; Morris, Sheldon L.; Jacobs, William R. Jr [Reprint Author]
CS Howard Hughes Med Inst, Albert Einstein Coll Med, 1300 Morris Pk Ave, Bronx, NY, 10461, USA
jacobsw@hhmi.org
SO Infection and Immunity, (February 2005) Vol. 73, No. 2, pp. 1196-1203. print.
ISSN: 0019-9567 (ISSN print).
DT Article
LA English
ED Entered STN: 4 May 2005
Last Updated on STN: 4 May 2005
AB We report the safety and immunogenicity of a double lysine and

pantothenate ***auxotroph*** of ***Mycobacterium*** tuberculosis in mice. The DELTAlysDELTA DELTApanCD mutant is completely attenuated in immunocompromised SCID and gamma interferon knockout mice yet induces short-term and long-term protection in immunocompetent and CD4-deficient mice following single-dose subcutaneous vaccination.

TI Long-term protection against tuberculosis following vaccination with a severely attenuated double lysine and ***pantothenate*** ***auxotroph*** of ***Mycobacterium*** tuberculosis.

AB We report the safety and immunogenicity of a double lysine and ***pantothenate*** ***auxotroph*** of ***Mycobacterium*** tuberculosis in mice. The DELTAlysDELTA DELTApanCD mutant is completely attenuated in immunocompromised SCID and gamma interferon knockout mice yet induces. . .

IT . . .
Immune System (Chemical Coordination and Homeostasis); Infection; Pharmacology

IT Diseases
tuberculosis: bacterial disease, drug therapy
Tuberculosis (MeSH)

IT Chemicals & Biochemicals
lysine- ***pantothenate*** double ***auxotroph*** vaccine: immunologic-drug, immunostimulant-drug, subcutaneous administration

ORGN . . .
Organism Name
mouse (common): host, strain-C57BL/6, strain-transgenic
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Rodents, Vertebrates

ORGN Classifier
Mycobacteriaceae 08881
Super Taxa
Mycobacteria ; Actinomycetes and Related Organisms; Eubacteria; Bacteria; Microorganisms
Organism Name
Mycobacterium tuberculosis (species): pathogen, strain-BCG-P, strain-H37Rv, strain-MC-26020
Taxa Notes
Bacteria, Eubacteria, Microorganisms

L19 ANSWER 28 OF 36 SCISEARCH COPYRIGHT (c) 2009 The Thomson Corporation on STN

AN 2005:723779 SCISEARCH <<LOGINID::20091103>>

GA The Genuine Article (R) Number: 941OP

TI Live attenuated mutants of ***Mycobacterium*** tuberculosis as candidate vaccines against tuberculosis

AU Jacobs W R (Reprint)

CS Yeshiva Univ Albert Einstein Coll Med, Howard Hughes Med Inst, Dept Microbiol & Immunol, 1300 Morris Pk Ave, Bronx, NY 10461 USA (Reprint)

AU Sambandamurthy V K

CS Yeshiva Univ Albert Einstein Coll Med, Howard Hughes Med Inst, Dept Microbiol & Immunol, Bronx, NY 10461 USA
E-mail: jacobsw@hhmi.org

CYA USA

SO MICROBES AND INFECTION, (MAY 2005) Vol. 7, No. 5-6, pp. 955-961.
ISSN: 1286-4579.

PB ELSEVIER SCIENCE BV, PO BOX 211, 1000 AE AMSTERDAM, NETHERLANDS.

DT Article; Journal
LA English
REC Reference Count: 32
ED Entered STN: 22 Jul 2005
Last Updated on STN: 22 Jul 2005
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB The recent advances in genetic tools to manipulate ***Mycobacterium*** tuberculosis have led to the construction of defined mutants and to the study of their role in the virulence and pathogenesis of tuberculosis. The safety and vaccine potential of a few of these M. tuberculosis mutants as candidate vaccines against tuberculosis are discussed. (c) 2005 Elsevier SAS. All rights reserved.
TI Live attenuated mutants of ***Mycobacterium*** tuberculosis as candidate vaccines against tuberculosis
AB The recent advances in genetic tools to manipulate ***Mycobacterium*** tuberculosis have led to the construction of defined mutants and to the study of their role in the virulence and. . .
ST Author Keywords: attenuated; double deletion ***pantothenate*** ; tuberculosis; vaccine
STP KeyWords Plus (R): CALMETTE-GUERIN; ***PANTOTHENATE*** ***AUXOTROPH*** ; GUINEA-PIGS; BOVIS BCG; PROTECTION; VIRULENCE; VACCINATION; INFECTION; EFFICACY; IMMUNITY

L19 ANSWER 29 OF 36 CAPLUS COPYRIGHT 2009 ACS on STN
AN 2005:455656 CAPLUS <<LOGINID::20091103>>
DN 143:340381
TI Identification and characterization of aconitase transcription regulators in Corynebacterium glutamicum
AU Krug, Andreas
CS Universitaet Duesseldorf, Duesseldorf, Germany
SO Schriften des Forschungszentrums Juelich, Reihe Lebenswissenschaften/Life Sciences (2005), 12, i-vi, 1-126
CODEN: SFLSF9; ISSN: 1433-5549
PB Forschungszentrum Juelich GmbH
DT Journal
LA German
AB Val-producing strains of Corynebacterium glutamicum were characterized by global expression anal. to identify target genes for optimization of a Val-producing strain. A repressor of aconitase (AcnR) was identified and characterized in C. glutamicum. Function was investigated of the transcriptional regulator NCgl0943. Influence was examd. of acn deletion and acn overexpression in C. glutamicum. A potential target gene for a putative transport protein was identified and its role in Val formation was analyzed by deletion and overexpression, but potential target genes for optimization of Val prodn. were not identified by comparing the transcriptomes of Val producers and Val non-producers. Three aconitase transcriptional regulators were identified in C. glutamicum. AcnR was supposed to be a repressor of acn expression. Two transcriptional start points of the acn gene were identified 110 and 113 bp upstream of the acn start codon by primer-extension anal. A putative consensus binding motif (CAGNACnnnnGTACTG) for AcnR was deduced by comparing acn promoter regions of Corynebacterium and ***Mycobacterium*** species. Mutations in this motif inhibited binding of AcnR on the acn promoter of C. glutamicum. RamA, a transcriptional regulator of genes involved in acetate metab. of C. glutamicum, was identified by DNA affinity chromatog. with the acn

promoter region. A transcriptional regulator of the AraC/XylS family (NCgl0943) was supposed to be responsible for Fe-dependent regulation of acn expression. A C. glutamicum strain with a deleted acn gene was glutamate- ***auxotrophic*** in Glc minimal medium, confirming the presence of one aconitase gene in C. glutamicum.

AB . . . primer-extension anal. A putative consensus binding motif (CAGNACnnnnGTACTG) for AcnR was deduced by comparing acn promoter regions of Corynebacterium and ***Mycobacterium*** species. Mutations in this motif inhibited binding of AcnR on the acn promoter of C. glutamicum. RamA, a transcriptional regulator. . . supposed to be responsible for Fe-dependent regulation of acn expression. A C. glutamicum strain with a deleted acn gene was glutamate- ***auxotrophic*** in Glc minimal medium, confirming the presence of one aconitase gene in C. glutamicum.

IT 79-83-4, ***Pantothenate***
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(***pantothenate*** effect on aconitase prodn. in Corynebacterium glutamicum)

L19 ANSWER 30 OF 36 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN DUPLICATE 4

AN 2004:338315 BIOSIS <<LOGINID::20091103>>

DN PREV200400338496

TI Protection elicited by a double leucine and ***pantothenate*** ***auxotroph*** of ***Mycobacterium*** tuberculosis in guinea pigs.

AU Sampson, Samantha L.; Dascher, Christopher C.; Sambandamurthy, Vasan K.; Russell, Robert G.; Jacobs, William R. Jr; Bloom, Barry R.; Hondalus, Mary K. [Reprint Author]

CS Sch Publ HlthDept Immunol and Infect Dis, Harvard Univ, 665 Huntington Ave, Boston, MA, 02115, USA
mhondalu@hsph.harvard.edu

SO Infection and Immunity, (May 2004) Vol. 72, No. 5, pp. 3031-3037. print.
ISSN: 0019-9567 (ISSN print).

DT Article

LA English

ED Entered STN: 11 Aug 2004
Last Updated on STN: 11 Aug 2004

AB We developed a live, fully attenuated ***Mycobacterium*** tuberculosis vaccine candidate strain with two independent attenuating ***auxotrophic*** mutations in leucine and ***pantothenate*** biosynthesis. The DELTAleuD DELTApanCD double ***auxotroph*** is fully attenuated in the SCID mouse model and highly immunogenic and protective in the extremely sensitive guinea pig tuberculosis model, reducing both bacterial burden and disease pathology.

TI Protection elicited by a double leucine and ***pantothenate*** ***auxotroph*** of ***Mycobacterium*** tuberculosis in guinea pigs.

AB We developed a live, fully attenuated ***Mycobacterium*** tuberculosis vaccine candidate strain with two independent attenuating ***auxotrophic*** mutations in leucine and ***pantothenate*** biosynthesis. The DELTAleuD DELTApanCD double ***auxotroph*** is fully attenuated in the SCID mouse model and highly immunogenic and protective in the extremely sensitive guinea pig tuberculosis. . .

ORGN . . .
immunodeficiency mouse (common): animal model, bacterial attenuation
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Rodents, Vertebrates

ORGN Classifier

Mycobacteriaceae 08881
Super Taxa
Mycobacteria ; Actinomycetes and Related Organisms; Eubacteria; Bacteria; Microorganisms
Organism Name
Mycobacterium tuberculosis (species): pathogen, double leucine mutant ***auxotroph*** , guinea pig vaccination, lung infection protection, ***pantothenate*** mutant ***auxotroph*** , severe combined immunodeficiency mouse attenuation
Taxa Notes
Bacteria, Eubacteria, Microorganisms

L19 ANSWER 31 OF 36 SCISEARCH COPYRIGHT (c) 2009 The Thomson Corporation on STN
AN 2004:837949 SCISEARCH <<LOGINID::20091103>>
GA The Genuine Article (R) Number: 853RQ
TI Tuberculosis vaccine development: research, regulatory and clinical strategies
AU Brennan M J (Reprint)
CS US FDA, Ctr Biol Evaluat & Res, Lab Mycobacterial Dis & Cellular Immunol, Bldg 29, Rm 503, HFM-431, 29 Lincoln Dr, Bethesda, MD 20892 USA (Reprint)
AU Morris S L; Sizemore C F
CS US FDA, Ctr Biol Evaluat & Res, Lab Mycobacterial Dis & Cellular Immunol, Bethesda, MD 20892 USA; NIAID, TB & Other Mycobacterial Dis Sect, Resp Dis Branch, Div Microbiol & Infect Dis, NIH, Bethesda, MD 20892 USA
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CYA USA
SO EXPERT OPINION ON BIOLOGICAL THERAPY, (SEP 2004) Vol. 4, No. 9, pp. 1493-1504.
ISSN: 1471-2598.
PB ASHLEY PUBLICATIONS LTD, UNITEC HOUSE, 3RD FL, 2 ALBERT PLACE, FINCHLEY CENTRAL, LONDON N3 1QB, ENGLAND.
DT General Review; Journal
LA English
REC Reference Count: 69
ED Entered STN: 15 Oct 2004
Last Updated on STN: 15 Oct 2004
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB In the past decade, while the global tuberculosis (TB) epidemic has continued to devastate mankind, considerable progress has nevertheless been made in the development of new and improved vaccines for this ancient disease. Recombinant bacillus Calmette-Guerin strains, DNA-based vaccines, live attenuated ***Mycobacterium*** tuberculosis vaccines and subunit vaccines formulated with novel adjuvants have shown promise in preclinical animal challenge models. Three of these vaccines are being evaluated at present in human clinical studies, and several other vaccine preparations are being targeted for clinical trials in the near future. Although the preclinical characterisation and testing of new TB vaccines has clearly led to exciting new findings, complex regulatory and clinical trial design issues remain as a challenge to TB vaccine development. This report reviews some of the exciting advances in TB research that have led to the development of new TB vaccines, and addresses the unique regulatory and clinical issues associated with the testing of novel anti-TB preparations in human populations.
AB . . . in the development of new and improved vaccines for this ancient disease. Recombinant bacillus Calmette-Guerin strains, DNA-based vaccines, live attenuated ***Mycobacterium*** tuberculosis vaccines

and subunit vaccines formulated with novel adjuvants have shown promise in preclinical animal challenge models. Three of these. . .

ST Author Keywords: ***Mycobacterium*** tuberculosis; tuberculosis vaccines; vaccine regulatory issues; vaccine trials

STP KeyWords Plus (R): BACILLUS-CALMETTE-GUERIN; ***MYCOBACTERIUM*** -TUBERCULOSIS; PROTECTIVE EFFICACY; BCG VACCINES; ENHANCED IMMUNOGENICITY; ***PANTOTHENATE*** ***AUXOTROPH*** ; IMMUNE-RESPONSES; RECENT PROGRESS; DNA; MICE

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AN 2004:58606 SCISEARCH <<LOGINID::20091103>>

GA The Genuine Article (R) Number: 759DP

TI ***Mycobacterium*** tuberculosis defective in phthiocerol dimycocerosate translocation provides greater protective immunity against tuberculosis than the existing bacille Calmette-Guerin vaccine

AU Triccas J A (Reprint)

CS Centenary Inst Canc Med & Cell Biol, Mycobacterial Res Grp, Locked Bag 6, Newtown, NSW 2042, Australia (Reprint)

AU Pinto R; Saunders B M; Camacho L R; Britton W J; Gicquel B

CS Centenary Inst Canc Med & Cell Biol, Mycobacterial Res Grp, Newtown, NSW 2042, Australia; Univ Sydney, Dept Med, Sydney, NSW 2006, Australia; Inst Pasteur, Unite Genet Mycobacterienne, Paris, France

CYA Australia; France

SO JOURNAL OF INFECTIOUS DISEASES, (1 JAN 2004) Vol. 189, No. 1, pp. 105-112. ISSN: 0022-1899.

PB UNIV CHICAGO PRESS, 1427 E 60TH ST, CHICAGO, IL 60637-2954 USA.

DT Article; Journal

LA English

REC Reference Count: 26

ED Entered STN: 23 Jan 2004
Last Updated on STN: 23 Jan 2004
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB We demonstrate that ***Mycobacterium*** tuberculosis that is unable to export the complex lipid phthiocerol dimycocerosate has a decreased capacity to replicate in mice and affords sustained protective immunity against M. tuberculosis infection Protection was significantly better than that provided by the existing vaccine, ***Mycobacterium*** bovis bacille Calmette-Guerin (BCG), and this improved protective efficacy was maintained for at least 24 weeks after vaccination. Protection afforded by this attenuated strain coincided with a number of factors that were not associated with BCG vaccination: long-term persistence of the strain within the host, sustained and potent induction of antimycobacterial interferon-gamma-secreting cells equal to that induced by virulent M. tuberculosis, and elicitation of T cells recognizing dominant M. tuberculosis antigens absent from BCG. These results suggest that the BCG vaccine may be too attenuated to afford effective protective immunity against tuberculosis, and vaccine strains that can provide sustained delivery of ***mycobacterial*** antigens are promising antituberculosis vaccine candidates.

TI ***Mycobacterium*** tuberculosis defective in phthiocerol dimycocerosate translocation provides greater protective immunity against tuberculosis than the existing bacille Calmette-Guerin vaccine

AB We demonstrate that ***Mycobacterium*** tuberculosis that is unable to export the complex lipid phthiocerol dimycocerosate has a decreased capacity to replicate in mice and affords sustained protective immunity against M. tuberculosis infection Protection was significantly better than

that provided by the existing vaccine, ***Mycobacterium*** bovis bacille Calmette-Guerin (BCG), and this improved protective efficacy was maintained for at least 24 weeks after vaccination. Protection afforded. . . may be too attenuated to afford effective protective immunity against tuberculosis, and vaccine strains that can provide sustained delivery of ***mycobacterial*** antigens are promising antituberculosis vaccine candidates.

STP KeyWords Plus (R): BOVIS BCG; INTERFERON-GAMMA; MICE; ATTENUATION; ***AUXOTROPH*** ; INFECTION; EFFICACY; DNA; ***RD1***

L19 ANSWER 33 OF 36 CAPLUS COPYRIGHT 2009 ACS on STN
AN 2003:678598 CAPLUS <<LOGINID::20091103>>
DN 139:212868
TI Attenuated ***Mycobacterium*** tuberculosis vaccines comprising deletion of ***RD1*** region
IN Jacobs, William R., Jr.; Hsu, Tsungda; Bardarov, Stoyan; Sambandamurthy, Vasan
PA Albert Einstein College of Medicine of Yeshiva University, USA
SO PCT Int. Appl., 102 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003070164	A2	20030828	WO 2003-US2046	20030124
	WO 2003070164	A3	20060216		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2003209345	A1	20030909	AU 2003-209345	20030124
PRAI	US 2002-358152P	P	20020219		
	WO 2003-US2046	W	20030124		

AB Non-naturally occurring ***mycobacteria*** in the ***Mycobacterium*** tuberculosis complex are provided. These ***mycobacteria*** have a deletion of an ***RD1*** region or a region controlling prodn. of a vitamin, and exhibit attenuated virulence in a mammal when compared to the ***mycobacteria*** without the deletion. Also provided are non-naturally occurring ***mycobacteria*** that have a deletion of a region controlling prodn. of lysine, and ***mycobacteria*** comprising two attenuating deletions. Vaccines comprising these ***mycobacteria*** are also provided, as are methods of protecting mammals from virulent ***mycobacteria*** using the vaccines. Also provided are methods of prepg. these vaccines which include the step of deleting an ***RD1*** region or a region controlling prodn. of a vitamin from a ***mycobacterium*** in the M tuberculosis complex.

OSC.G 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Attenuated ***Mycobacterium*** tuberculosis vaccines comprising deletion of ***RD1*** region

AB Non-naturally occurring ***mycobacteria*** in the ***Mycobacterium*** tuberculosis complex are provided. These ***mycobacteria*** have a deletion of an ***RD1*** region or a region controlling prodn. of a vitamin, and exhibit attenuated virulence in a mammal when compared to the ***mycobacteria*** without the deletion. Also provided are non-naturally occurring ***mycobacteria*** that have a deletion of a region controlling prodn. of lysine, and ***mycobacteria*** comprising two attenuating deletions. Vaccines comprising these ***mycobacteria*** are also provided, as are methods of protecting mammals from virulent ***mycobacteria*** using the vaccines. Also provided are methods of prepg. these vaccines which include the step of deleting an ***RD1*** region or a region controlling prodn. of a vitamin from a ***mycobacterium*** in the M tuberculosis complex.

ST ***Mycobacterium*** tuberculosis vitamin pantothenic acid NAD ***RD1*** region deletion; antigen vaccine ***Mycobacterium*** tuberculosis ***RD1*** deletion

IT Borrelia
Bos taurus
DNA sequences
Genetic engineering
Genetic markers
Herpesviridae
Human
Human immunodeficiency virus
Human poliovirus
Immunodeficiency
Immunostimulants
Infection
Leishmania
Mammalia
Measles virus
Molecular cloning
Mumps virus
Mus
Mycobacterium BCG
Mycobacterium africanum
Mycobacterium avium
Mycobacterium bovis
Mycobacterium intracellulare
Mycobacterium leprae
Mycobacterium tuberculosis
Neisseria
Pertussis
Rabies
Recombination, genetic
Salmonella
Shigella
Transduction, genetic
Treponema
Vaccines
Vibrio cholerae
(attenuated ***Mycobacterium*** tuberculosis comprising deletion of ***RD1*** region for vaccine prepns.)

IT Vitamins

RL: BSU (Biological study, unclassified); REM (Removal or disposal); BIOL (Biological study); PROC (Process)
(attenuated ***Mycobacterium*** tuberculosis comprising deletion of ***RD1*** region for vaccine prepns.)

IT Antigens
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(attenuated ***Mycobacterium*** tuberculosis comprising deletion of ***RD1*** region for vaccine prepns.)

IT Enzymes, biological studies
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(attenuated ***Mycobacterium*** tuberculosis comprising deletion of ***RD1*** region for vaccine prepns.)

IT Interleukin 1
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(attenuated ***Mycobacterium*** tuberculosis comprising deletion of ***RD1*** region for vaccine prepns.)

IT Interleukin 2
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(attenuated ***Mycobacterium*** tuberculosis comprising deletion of ***RD1*** region for vaccine prepns.)

IT Interleukin 3
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(attenuated ***Mycobacterium*** tuberculosis comprising deletion of ***RD1*** region for vaccine prepns.)

IT Interleukin 4
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(attenuated ***Mycobacterium*** tuberculosis comprising deletion of ***RD1*** region for vaccine prepns.)

IT Interleukin 5
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(attenuated ***Mycobacterium*** tuberculosis comprising deletion of ***RD1*** region for vaccine prepns.)

IT Interleukin 6
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(attenuated ***Mycobacterium*** tuberculosis comprising deletion of ***RD1*** region for vaccine prepns.)

IT Interleukin 7
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(attenuated ***Mycobacterium*** tuberculosis comprising deletion of ***RD1*** region for vaccine prepns.)

IT Lymphokines
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(attenuated ***Mycobacterium*** tuberculosis comprising deletion of ***RD1*** region for vaccine prepns.)

IT Lymphotoxin
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(attenuated ***Mycobacterium*** tuberculosis comprising deletion of ***RD1*** region for vaccine prepns.)

IT Reporter gene
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(attenuated ***Mycobacterium*** tuberculosis comprising deletion of ***RD1*** region for vaccine prepns.)

IT Tumor necrosis factors
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(attenuated ***Mycobacterium*** tuberculosis comprising deletion of ***RD1*** region for vaccine prepns.)

IT Microorganism
(***auxotrophic*** ; attenuated ***Mycobacterium*** tuberculosis comprising deletion of ***RD1*** region for vaccine prepns.)

IT Development, mammalian postnatal
(child; attenuated ***Mycobacterium*** tuberculosis comprising deletion of ***RD1*** region for vaccine prepns.)

IT Toxoids
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(diphtheria; attenuated ***Mycobacterium*** tuberculosis comprising deletion of ***RD1*** region for vaccine prepns.)

IT Steroids, biological studies
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(enzyme; attenuated ***Mycobacterium*** tuberculosis comprising deletion of ***RD1*** region for vaccine prepns.)

IT Drug delivery systems
(injections, s.c.; attenuated ***Mycobacterium*** tuberculosis comprising deletion of ***RD1*** region for vaccine prepns.)

IT Venoms
(insect; attenuated ***Mycobacterium*** tuberculosis comprising deletion of ***RD1*** region for vaccine prepns.)

IT Drug delivery systems
(intradermal; attenuated ***Mycobacterium*** tuberculosis comprising deletion of ***RD1*** region for vaccine prepns.)

IT Development, microbial
(merozoite, malaria; attenuated ***Mycobacterium*** tuberculosis comprising deletion of ***RD1*** region for vaccine prepns.)

IT DNA
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(recombinant; attenuated ***Mycobacterium*** tuberculosis comprising deletion of ***RD1*** region for vaccine prepns.)

IT Gene, microbial
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(sacB; attenuated ***Mycobacterium*** tuberculosis comprising deletion of ***RD1*** region for vaccine prepns.)

IT Mutagenesis
(site-directed, deletion; attenuated ***Mycobacterium*** tuberculosis comprising deletion of ***RD1*** region for vaccine prepns.)

IT Venoms
(snake; attenuated ***Mycobacterium*** tuberculosis comprising deletion of ***RD1*** region for vaccine prepns.)

IT Development, microbial
(sporozoite, malaria; attenuated ***Mycobacterium*** tuberculosis comprising deletion of ***RD1*** region for vaccine prepns.)
IT Toxoids
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tetanus; attenuated ***Mycobacterium*** tuberculosis comprising deletion of ***RD1*** region for vaccine prepns.)
IT Tuberculosis
(vaccine; attenuated ***Mycobacterium*** tuberculosis comprising deletion of ***RD1*** region for vaccine prepns.)
IT Insecta
(venom; attenuated ***Mycobacterium*** tuberculosis comprising deletion of ***RD1*** region for vaccine prepns.)
IT Interferons
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(.alpha.; attenuated ***Mycobacterium*** tuberculosis comprising deletion of ***RD1*** region for vaccine prepns.)
IT Interferons
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(.beta.; attenuated ***Mycobacterium*** tuberculosis comprising deletion of ***RD1*** region for vaccine prepns.)
IT Interferons
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(.gamma.; attenuated ***Mycobacterium*** tuberculosis comprising deletion of ***RD1*** region for vaccine prepns.)
IT 53-84-9, Nicotinamide adenine dinucleotide 56-87-1, L-Lysine, biological studies 61-90-5, L-Leucine, biological studies 73-22-3, L-Tryptophan, biological studies 79-83-4, Pantothenic acid 147-85-3, L-Proline, biological studies
RL: BSU (Biological study, unclassified); REM (Removal or disposal); BIOL (Biological study); PROC (Process)
(attenuated ***Mycobacterium*** tuberculosis comprising deletion of ***RD1*** region for vaccine prepns.)
IT 9001-45-0, .beta. Glucuronidase 9014-00-0, Luciferase 9031-11-2, .beta. Galactosidase 63774-46-9
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(attenuated ***Mycobacterium*** tuberculosis comprising deletion of ***RD1*** region for vaccine prepns.)
IT 588746-25-2P
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(nucleotide sequence; attenuated ***Mycobacterium*** tuberculosis comprising deletion of ***RD1*** region for vaccine prepns.)
IT 588746-26-3 588746-27-4 588746-28-5
RL: BSU (Biological study, unclassified); PRP (Properties); REM (Removal or disposal); BIOL (Biological study); PROC (Process)
(nucleotide sequence; attenuated ***Mycobacterium*** tuberculosis comprising deletion of ***RD1*** region for vaccine prepns.)
IT 588747-89-1 588747-90-4 588747-91-5 588747-92-6 588747-93-7 588747-94-8 588747-95-9 588747-96-0
RL: PRP (Properties)

(unclaimed nucleotide sequence; attenuated ***Mycobacterium*** tuberculosis vaccines comprising deletion of ***RD1*** region)

L19 ANSWER 34 OF 36 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN DUPLICATE 5
AN 2002:600487 BIOSIS <<LOGINID::20091103>>
DN PREV200200600487
TI Specialized transduction: An efficient method for generating marked and unmarked targeted gene disruptions in ***Mycobacterium*** tuberculosis, M. bovis BCG and M. smegmatis.
AU Bardarov, Stoyan; Bardarov, Svetoslav; Pavelka, Martin S., Jr.; Sambandamurthy, Vasan; Larsen, Michelle; Tufariello, JoAnn; Chan, John; Hatfull, Graham; Jacobs, William R., Jr. [Reprint author]
CS Dept of Microbiology and Immunology, Howard Hughes Medical Institute, Albert Einstein College of Medicine, Bronx, NY, 10461, USA
jacobsw@hhmi.org
SO Microbiology (Reading), (October, 2002) Vol. 148, No. 10, pp. 3007-3017. print.
ISSN: 1350-0872.
DT Article
LA English
ED Entered STN: 20 Nov 2002
Last Updated on STN: 20 Nov 2002
AB The authors have developed a simple and highly efficient system for generating allelic exchanges in both fast- and slow-growing ***mycobacteria*** . In this procedure a gene of interest, disrupted by a selectable marker, is cloned into a conditionally replicating (temperature-sensitive) shuttle phasmid to generate a specialized transducing ***mycobacteriophage*** . The temperature-sensitive mutations in the ***mycobacteriophage*** genome permit replication at the permissive temperature of 30degreeC but prevent replication at the non-permissive temperature of 37degreeC. Transduction at a non-permissive temperature results in highly efficient delivery of the recombination substrate to virtually all cells in the recipient population. The deletion mutations in the targeted genes are marked with antibiotic-resistance genes that are flanked by gammadelta-res (resolvase recognition target) sites. The transductants which have undergone a homologous recombination event can be conveniently selected on antibiotic-containing media. To demonstrate the utility of this genetic system seven different targeted gene disruptions were generated in three substrains of ***Mycobacterium*** bovis BCG, three strains of ***Mycobacterium*** tuberculosis, and ***Mycobacterium*** smegmatis.
Mutants in the lysA, nadBC, panC, ***panCD*** , leuCD, Rv3291c and Rv0867c genes or operons were isolated as antibiotic-resistant (and in some cases ***auxotrophic***) transductants. Using a plasmid encoding the gammadelta-resolvase (tnpR), the resistance genes could be removed, generating unmarked deletion mutations. It is concluded from the high frequency of allelic exchange events observed in this study that specialized transduction is a very efficient technique for genetic manipulation of ***mycobacteria*** and is a method of choice for constructing isogenic strains of M. tuberculosis, BCG or M. smegmatis which differ by defined mutations.
TI Specialized transduction: An efficient method for generating marked and unmarked targeted gene disruptions in ***Mycobacterium*** tuberculosis, M. bovis BCG and M. smegmatis.
AB The authors have developed a simple and highly efficient system for

generating allelic exchanges in both fast- and slow-growing ***mycobacteria*** . In this procedure a gene of interest, disrupted by a selectable marker, is cloned into a conditionally replicating (temperature-sensitive) shuttle phasmid to generate a specialized transducing ***mycobacteriophage*** . The temperature-sensitive mutations in the ***mycobacteriophage*** genome permit replication at the permissive temperature of 30degreeC but prevent replication at the non-permissive temperature of 37degreeC. Transduction at. . . media. To demonstrate the utility of this genetic system seven different targeted gene disruptions were generated in three substrains of ***Mycobacterium*** bovis BCG, three strains of ***Mycobacterium*** tuberculosis, and ***Mycobacterium*** smegmatis. Mutants in the lysA, nadBC, panC, ***panCD*** , leuCD, Rv3291c and Rv0867c genes or operons were isolated as antibiotic-resistant (and in some cases ***auxotrophic***) transductants. Using a plasmid encoding the gammadelta-resolvase (tnpR), the resistance genes could be removed, generating unmarked deletion mutations. It is. . . of allelic exchange events observed in this study that specialized transduction is a very efficient technique for genetic manipulation of ***mycobacteria*** and is a method of choice for constructing isogenic strains of M. tuberculosis, BCG or M. smegmatis which differ by. . .

ORGN . . .

Taxa

Primates; Mammalia; Vertebrata; Chordata; Animalia

Organism Name

human: host

Taxa Notes

Animals, Chordates, Humans, Mammals, Primates, Vertebrates

ORGN Classifier

Mycobacteriaceae 08881

Super Taxa

Mycobacteria ; Actinomycetes and Related Organisms; Eubacteria; Bacteria; Microorganisms

Organism Name

Mycobacterium bovis BCG: pathogen

Mycobacterium bovis smegmatis: pathogen

Mycobacterium tuberculosis: pathogen

Taxa Notes

Bacteria, Eubacteria, Microorganisms

GEN ***Mycobacterium*** Rv0867c gene (***Mycobacteriaceae***);
Mycobacterium Rv3291c gene (***Mycobacteriaceae***);
Mycobacterium leuCD gene (***Mycobacteriaceae***);
Mycobacterium lysA gene (***Mycobacteriaceae***);
Mycobacterium nadBC gene (***Mycobacteriaceae***);
Mycobacterium panC gene (***Mycobacteriaceae***);
Mycobacterium ***panCD*** gene (***Mycobacteriaceae***)

L19 ANSWER 35 OF 36 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN DUPLICATE 6

AN 2002:542024 BIOSIS <<LOGINID::20091103>>

DN PREV200200542024

TI A ***pantothenate*** ***auxotroph*** of ***Mycobacterium*** tuberculosis is highly attenuated and protects mice against tuberculosis.

AU Sambandamurthy, Vasan K.; Wang, Xiaojuan; Chen, Bing; Russell, Robert G.; Derrick, Steven; Collins, Frank M.; Morris, Sheldon L.; Jacobs, William R., Jr. [Reprint author]

CS Department of Microbiology and Immunology, Howard Hughes Medical

Institute, Bronx, NY, USA
jacobsw@hhmi.org
SO Nature Medicine, (October, 2002) Vol. 8, No. 10, pp. 1171-1174. print.
ISSN: 1078-8956.
DT Article
LA English
ED Entered STN: 23 Oct 2002
Last Updated on STN: 23 Oct 2002
AB With the advent of HIV and the widespread emergence of drug-resistant strains of ***Mycobacterium*** tuberculosis, newer control strategies in the form of a better vaccine could decrease the global incidence of tuberculosis. A desirable trait in an effective live attenuated vaccine strain is an ability to persist within the host in a limited fashion in order to produce important protective antigens in vivo. Attenuated M. tuberculosis vaccine candidates have been constructed by deleting genes required for growth in mice. These candidate vaccines did not elicit adequate protective immunity in animal models, due to their inability to persist sufficiently long within the host tissues. Here we report that an ***auxotrophic*** mutant of M. tuberculosis defective in the de novo biosynthesis of pantothenic acid (vitamin B5) is highly attenuated in immunocompromised SCID mice and in immunocompetent BALB/c mice. SCID mice infected with the ***pantothenate*** ***auxotroph*** survived significantly longer (250 days) than mice infected with either bacille Calmette-Guerin (BCG) vaccine or virulent M. tuberculosis (77 and 35 days, respectively). Subcutaneous immunization with this ***auxotroph*** conferred protection in C57BL/6J mice against an aerosol challenge with virulent M. tuberculosis, which was comparable with that afforded by BCG vaccination. Our findings highlight the importance of de novo ***pantothenate*** biosynthesis in limiting the intracellular survival and pathogenesis of M. tuberculosis without reducing its immunogenicity in vaccinated mice.
TI A ***pantothenate*** ***auxotroph*** of ***Mycobacterium*** tuberculosis is highly attenuated and protects mice against tuberculosis.
AB With the advent of HIV and the widespread emergence of drug-resistant strains of ***Mycobacterium*** tuberculosis, newer control strategies in the form of a better vaccine could decrease the global incidence of tuberculosis. A desirable. . . in animal models, due to their inability to persist sufficiently long within the host tissues. Here we report that an ***auxotrophic*** mutant of M. tuberculosis defective in the de novo biosynthesis of pantothenic acid (vitamin B5) is highly attenuated in immunocompromised SCID mice and in immunocompetent BALB/c mice. SCID mice infected with the ***pantothenate*** ***auxotroph*** survived significantly longer (250 days) than mice infected with either bacille Calmette-Guerin (BCG) vaccine or virulent M. tuberculosis (77 and 35 days, respectively). Subcutaneous immunization with this ***auxotroph*** conferred protection in C57BL/6J mice against an aerosol challenge with virulent M. tuberculosis, which was comparable with that afforded by BCG vaccination. Our findings highlight the importance of de novo ***pantothenate*** biosynthesis in limiting the intracellular survival and pathogenesis of M. tuberculosis without reducing its immunogenicity in vaccinated mice.
IT Major Concepts
Immune System (Chemical Coordination and Homeostasis); Infection
IT Diseases
tuberculosis: bacterial disease, epidemiology
Tuberculosis (MeSH)
IT Chemicals & Biochemicals

Mycobacterium tuberculosis vaccine: immunologic-drug, immunostimulant-drug; ***pantothenate*** : biosynthesis

ORGN . . .
Chordata; Animalia
Organism Name
mouse: host, immunocompromised
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Rodents, Vertebrates
ORGN Classifier
Mycobacteriaceae 08881
Super Taxa
Mycobacteria ; Actinomycetes and Related Organisms; Eubacteria; Bacteria; Microorganisms
Organism Name
Mycobacterium tuberculosis: ***auxotroph***
Taxa Notes
Bacteria, Eubacteria, Microorganisms
RN 20938-62-9 (***pantothenate***)

L19 ANSWER 36 OF 36 SCISEARCH COPYRIGHT (c) 2009 The Thomson Corporation on STN
AN 2003:104040 SCISEARCH <<LOGINID::20091103>>
GA The Genuine Article (R) Number: 636DP
TI A ***pantothenate*** ***auxotroph*** of ***Mycobacterium*** tuberculosis is highly attenuated and protects mice against tuberculosis.
AU ANON
CS CEA, U548 INSERM, F-38054 Grenoble, France; Univ Basel, Pharmactr, Dept Immunol, CH-4065 Basel, Switzerland
SO NATURE REVIEWS IMMUNOLOGY, (OCT 2002) Vol. 2, No. 10, pp. 719-719. ISSN: 1474-1733.
PB NATURE PUBLISHING GROUP, MACMILLAN BUILDING, 4 CRINAN ST, LONDON N1 9XW, ENGLAND.
DT News Announcement; Journal
LA English
REC Reference Count: 0
ED Entered STN: 7 Feb 2003
Last Updated on STN: 7 Feb 2003
TI A ***pantothenate*** ***auxotroph*** of ***Mycobacterium*** tuberculosis is highly attenuated and protects mice against tuberculosis.